



DISINHIBITION AND ALCOHOL CONSUMPTION

Thesis submitted in accordance with the requirements of the University
of Liverpool for the degree of Doctor in Philosophy by Andrew Jones

September 2012

Contents

Chapter One: General Introduction	Page: 1
1.1 Alcohol use: definitions, prevalence and statistics	1
1.2 Use, abuse and dependence	3
1.3 Addiction characterised as loss of control	5
1.4. Disinhibition and Response Inhibition	
1.4.1 Definition	6
1.4.2 Measuring Disinhibition: Behavioural Tasks	7
1.4.3 Development and Neural components	10
1.5.1 Impulsivity and Executive Function theories of addiction	12
1.5.2 Disinhibition in substance use	15
1.5.3 Neuropsychophysiological associations	16
1.6 Neurobiological theories: disinhibition as a consequence of chronic drug use	18
1.7 Longitudinal theories: disinhibition as a risk factor	21
1.8 Dual process theories: disinhibition as a possible mediator of the influence of other processes on drug use and abuse	23
1.9 State changes in (dis)inhibition	26
1.10 Limited resource models: possible evidence of state fluctuations	26
1.11 Acute alcohol consumption and disinhibition	29
1.12 Motivations and Beliefs: Drinking restraint	31
1.13 Interim summary	33
1.14 Experimental evidence of transient disinhibition in drug using populations	35
1.15 Hypothesis and Aims	36
Chapter Two: General methods	38
2.1 Questionnaires	38
2.2 Bogus taste test / <i>ad-libitum</i> alcohol session	42
Chapter Three: Priming a restrained mental set reduces alcohol-seeking independently of mood.	44
3.1 Abstract	45
3.2 Introduction	46
3.3 Method	48

3.4	Results	51
3.5	Discussion	55
Chapter Four: P300 during response inhibition is associated with ad-lib alcohol consumption in social drinkers		70
4.1	Abstract	71
4.2	Introduction	72
4.3	Method	74
4.4	Results	78
4.5	Discussion	80
4.6	Supplementary Analysis	83
Chapter Five: The effects of cue-specific inhibition training on alcohol consumption in heavy social drinkers		91
5.1	Abstract	92
5.2	Introduction	93
5.3	Experiment one	95
5.4	Method	96
5.5	Results	99
5.6	Experiment two	102
5.7	Method	103
5.8	Results	105
5.9	Discussion	107
5.10	Supplementary Materials	110
Chapter Six: Effects of alcohol cues on craving and <i>ad-libitum</i> alcohol consumption in social drinkers: the role of disinhibition.		117
6.1	Abstract	118
6.2	Introduction	119
6.3	Method	121
6.4	Results	124
6.5	Discussion	128
Chapter Seven: The effect of restraint beliefs on alcohol-seeking behaviour		137
7.1	Abstract	138
7.2	Introduction	139
7.3	Method	141

7.4	Results	144
7.5	Discussion	146
	Chapter Eight: General Discussion	150
	Summary of main findings	
8.1.1	Behavioural disinhibition	150
8.1.2	Oculomotor disinhibition	157
8.1.3	Restraint beliefs	159
8.2	Individual differences in disinhibition and their association with <i>ad-libitum</i> alcohol consumption in the laboratory	160
8.3	Overall support of theoretical models of disinhibition in addiction	161
8.4	Overall support for relevant models of restraint beliefs in addiction	163
8.5	Comparisons between ‘state’ and ‘trait’ disinhibition	164
	Limitations	
8.6.1	Generalisation to those motivated to reduce drinking	165
8.6.2	Task properties	166
8.7	Future research	168
8.8	Clinical applications of these findings	169
8.9	Concluding Comments	170
	References	172

List of Figures

3.1	Beer consumption (as a percentage of total fluid consumed) among participants in Control, Disinhibition, and Restraint Groups.	64
4.1	Grand average isopotential maps and a comparison of ERPs along the midline electrodes for both conflict and restraint conditions.	87
4.2	The intracorrelations between P300 amplitude, SSRT and beer consumption for both conflict and restraint conditions.	88
4.S.1	Supplementary Analyses: Source dipole analyses.	90
5.1	Beer as a percentage of total fluid consumed for experimental groups following the cued stop-signal task, in Experiment One.	112
6.1	Positive and negative urge over time.	135
6.2	Alcohol consumption during the taste test.	136
7.1	Group differences in beer consumption (as a percentage of total fluid consumed) during the bogus taste test.	155

List of Tables

3.1	Characteristics of participants allocated to Control, Disinhibition and Restraint groups.	60
3.2	Performance on the stop-signal task, shown separately for Control, Disinhibition, and Restraint groups.	61
3.3	Heart rate, blood pressure, self-reported mood and alcohol craving, shown separately for Control, Disinhibition, and Restraint groups, before and after completion of the stop-signal task.	62
3.4	Participant responses to the stop-signal task.	63
3.S.1	Characteristics of participants allocated to Control, Disinhibition and Restraint groups, split by gender.	65
3.S.2	Performance on the stop-signal task, shown separately for Control, Disinhibition, and Restraint groups, split by gender.	66
3.S.3	Heart rate, blood pressure, self-reported mood and alcohol craving, shown separately for Control, Disinhibition, and Restraint groups, before and after completion of the stop-signal task, split by gender.	67
3.S.4	Participant responses to the stop-signal task, split by gender.	68
3.S.5	Fluid consumed during the taste test and pleasantness ratings, split by gender.	69
4.1	Dependent measures from the stop-signal task, shown separately across conditions.	86
5.1	Reaction times and proportion of inhibition errors over time, shown separately for groups, across Experiment One and Two.	113
5.S.1	Participant characteristics in Experiment One.	114
5.S.2	Self-reported mood and alcohol craving before and after completion of the inhibitory control manipulations, in Experiments One and Two.	115
5.S.3	Participant characteristics in Experiment Two.	116
6.1	Participant characteristics between groups.	131
6.2	Post-task feedback scales at post-sniffing and post-stop-signal task assessments.	132
6.3	Self-reported mood and alcohol craving, shown separately for Group at baseline, after cue exposure and after the stop-signal task.	133

6.4	Performance on the Stop-signal task, shown separately for group.	134
7.1	Characteristics of participants allocated to high and low restraint groups.	148

This thesis is submitted in partial fulfilment of the conditions for a PhD by published papers. In accordance with the University of Liverpool guidelines and regulations the experimental chapters (Chapters Three to Seven) of this thesis will take the form of journal article manuscripts, which have either been published during the preparation of this thesis, or are under review in a peer-reviewed journal. Specific details with regards to journal submission and contribution of authors are given at the beginning of each chapter, as required.

Disinhibition and alcohol consumption

Andrew Jones

Abstract

The current thesis aimed to explore the relationship between disinhibition and alcohol consumption in non-dependent drinkers. Specifically, whether (dis)inhibition can be considered a ‘state’ variable, which is responsive to motivational biases, cues and training. It was examined whether any fluctuations in (dis)inhibition could influence subsequent *ad-libitum* alcohol consumption, in sober individuals (de Wit, 2009). Furthermore, the effects of beliefs about disinhibition, exclusively in relation to alcohol-seeking, were also examined with respect to possible effects on alcohol-seeking. These general research questions were examined in a heavy drinking, student population.

Chapter One discussed in detail the relationship between disinhibition and alcohol consumption by examining evidence from relevant models of addiction. Chapter Two described the general methods used in the experimental chapters of the thesis. In the first experimental chapter (Chapter Three) individuals were primed with different motivational biases on how to respond on a stop-signal task, before *ad-libitum* consumption was measured. Different motivational biases led to group differences in inhibition performance, it was demonstrated that a restrained mental set led to a reduction in alcohol consumption in the laboratory. Expanding this finding, Chapter Four examined the effect of these motivational biases on neuropsychophysiological measures (Event Related Potentials and Source dipole analyses) of inhibitory control; associations between inhibition indices and *ad-libitum* consumption were discussed. Chapter Five set out to examine whether inhibitory control could be trained specifically to alcohol cues, and whether this training could serve to reduce alcohol consumption in the laboratory (Experiment One and Two) and outside the laboratory (Experiment One) in response to emerging research (Houben et al 2011a). Two different types of inhibition training, motor and oculomotor, were compared in this chapter. Results demonstrated some success for motor, but not oculomotor inhibition, in both training behaviour and reductions in alcohol consumption, highlighting the fundamental differences in these constructs. Chapter Six examined whether alcohol cues could cause disinhibition in heavy social

drinkers, but found no evidence for cue-related disinhibition. However, some evidence for disinhibition and cue-reactivity was established and possible methodological issues discussed. In the final experimental chapter (Chapter Seven) restraint beliefs were examined in relation to *ad-libitum* alcohol consumption. It was found that beliefs could influence *ad-libitum* alcohol-seeking, however results were at first glance paradoxical to behavioural research.

The overall results of this thesis offer some of the first experimental support for the causal relationship between state disinhibition and alcohol consumption in sober, non-dependent individuals. Support was offered for the theories of addiction that postulate the association between disinhibition and alcohol consumption, specifically recent models that suggest disinhibition is a state which can influence drinking behaviour. Finally, support for recent theories that suggest targeting controlled processes may serve to reduce alcohol consumption in populations at high risk for alcohol abuse.

Declaration

No portion of this work has been submitted in support of any other application for degree or qualification at this or any other University or institute of learning.

Acknowledgements

Thanks to Matt Field, who gave me the opportunity to study for this PhD, as well as his help and advice during the last few years. Also, to Andrew Goudie, Abi Rose, Andrej Stancak, Paul Christiansen and Jon Cole who have all provided their supervision, time and/or expertise at some point. Special thanks to my Mum and Dad for their constant support and to Emma for putting up with me. Without these people this thesis would not have been possible.

A final thank you to all the psychology dept. at the University of Liverpool, my experimental subjects, journal editors and peer reviewers.

Chapter One

General Introduction

1.1. Alcohol use: definitions, prevalence and statistics

According to the World Health Organisation's global status report (WHO 2011), up to one billion people consume alcohol world wide; this is second only to caffeine in terms of psychoactive substance use. The latest data (2005) suggests that on an international scale, individuals over 15 years old consume around 6 litres of pure alcohol per annum. Globally, harmful alcohol use contributes to over 2.5 million fatalities every year, or approximately 4% of yearly deaths. Alcohol has a causal influence on at least 60 types of disease and injury and possibly contributes to around 200 others. Overall consumption and the problems associated differ greatly across regions, with higher income countries reporting the greatest consumption of alcohol - Europe has a much higher rate of consumption, around 9.5 litres of pure alcohol per annum, compared to less than 1 litre in African and South-east Asian regions (WHO).

In the UK, National Health Service statistics suggest that over 69% of men and 55% of women over 18 drink socially, as defined by at least one alcoholic drink per week (NHS 2011). Motives for social drinking are generally driven by alcohol's short-term subjective and pharmacological effects, which can increase positive and reduce negative affect (Cox and Klinger 1988; Mohr et al. 2005). Specific effects of acute alcohol consumption can include social lubrication through peer approval (Cox and Klinger 1988), an increased likelihood of sexual activity and perceived stress reduction (Sayette 1993). The British Household Panel Survey (BHPS 2006) reports that the average weekly alcohol consumption is 9.2 units for females and 19.9 units for males (1 UK unit = 25ml of a standard spirit = 8 grams of pure alcohol). Whilst the majority of adults in the United Kingdom drink alcohol, an increasing number of individuals are drinking more than is recommended by the Department Of Health; 14

units per week for women and 21 units for men. National statistics from the Information Centre for Health and Social Care suggest that 26% of men and 18% of women report drinking above these limits regularly (ICHSC 2011). According to Adult Psychiatric Morbidity Survey (2007), the prevalence of 'hazardous' drinking, as defined by the Alcohol Use Disorders Identification Test (AUDIT; Saunders et al. 1993) stands at close to one quarter of the UK's population.

In young adults the incidence of harmful drinking is comparatively greater. Prevalence of hazardous drinking in women is highest at ages 16 to 19 (23%) and in men, at ages 19 to 24 (63%), according to the Office of National Statistics (ONS 2002). This is especially concerning when it is considered that in Europe, over 35% of male deaths between the ages of 15 to 29 are alcohol-attributable (WHO 2011), and over 320,000 of the 2.5 million annual deaths are individuals aged 29 and under. A large proportion of young adults who attend university in the UK (61% of male, 48% of female), drink more than the recommendations put forward by the Department of Health (Webb et al. 1996). With specific regard to university students the pattern of increased, harmful drinking is driven largely by alcohol bingeing. Again, a significant proportion of young adults aged 16 to 24, comprising 42% men and 39% women are participating in at least one heavy episodic drinking session (binge) per week.

Alcohol use can cause disease and injury to the individual, both in the short and long term. Acute alcohol intoxication can have a variety of effects from memory impairments to severe respiratory depression. The adverse effects of chronic alcohol consumption include cirrhosis of the liver, epilepsy, poisonings and 3.6% of cancers, including liver and stomach (Boffetta et al. 2006). As well as physical health, alcohol consumption increases the risk of a variety of mental illnesses, such as depression (Fergusson et al. 2009). At 10%, the burden of disease attributable to alcohol, i.e. the impact of a health problem measured by cost and morbidity, is second only to smoking in relation to the adverse affects of addictive substances according to the Alcohol Needs Assessment Research Project (ANARP 2004).

Alcohol misuse is not only harmful to the individual but also to society, with hospital admissions as a direct consequence of alcohol costing the National Health Service approximately £168 million per annum, with admissions partially attributed to

alcohol (e.g. fighting whilst intoxicated) increasing this figure to £2.7 billion. Direct costs to the government and industry through alcohol related crime and costs incurred by workdays lost per year to 'hangover' related illness, place a further burden upon the economy, with one in 26 'bed days' in the UK being attributed to alcohol-related illness according to the Prime Minister's Strategy Unit (PMSU 2004).

The population and cost statistics presented serve to highlight the problems associated with alcohol misuse on a global and national scale. However, significant variance in drinking behaviour exists within populations. The quantity and frequency of alcohol use, as well as the problems it may cause, may assist in categorising individuals according to their risk of alcohol related problems.

1.2. Use, abuse and dependence

Using the Diagnostic and Statistical Manual of Mental Disorders IV (DSM-IV), individuals can be categorized according to the severity of symptoms associated with their alcohol use. In a clinical setting, i.e. individuals referred to or seeking treatment for their alcohol use, their behaviour may be labelled as substance abuse or substance dependence. For behaviour to be labelled as substance abuse, an individual's drinking behaviour must have led to one or more of the following symptoms in the past 12 months:

- Failure to fulfil major obligation (e.g. absence from work)
- Substance use under physically hazardous conditions (e.g. driving a car)
- Legal problems as a result of substance use
- Or recurrent social/personal problems due to substance use.

For behaviour to be classified as substance dependence, individuals must fulfil at least three of the following symptoms in the past 12 months:

- Tolerance to drug effect (same amount of drug has a diminished effect or more of the substance is needed to achieve the same effect)
- Withdrawal
- Increased use over longer period of time than planned
- A persistent desire and/or to control substance intake
- Increased time spent procuring the substance or recovering from the effects
- Reduction of other social/occupational/recreational activities to focus on substance use
- And/or continued use in the knowledge that it is exacerbating a physical or psychological problem.

Alcohol abuse can be seen as a precursor to dependence, which is characterised as a physical or mental addiction to alcohol. The DSM-IV states that there can be no overlap between abuse and dependence for any specific substance, outlining a distinction between the two.

The development of the DSM-V (which is due for publication in May 2013) will lead to significant changes in the labels of these disorders. For example, a key proposed revision is that alcohol abuse and dependence be subsumed under a new label: 'alcohol (or substance) use disorder'. The rationale behind this is that whilst the test-retest reliability of 'dependence' was high, the reliability of abuse was much more variable and that although abuse is seen as a precursor to dependence this is not always the case (Hasin et al. 2003). In the DSM-V Alcohol use disorder will be graded on clinical severity, following diagnosis based on similar criteria for abuse and dependence (however, individuals will need to exhibit only two symptoms over a twelve month period).

Whilst a large proportion (over 30%) of heavy drinking students fulfil the criteria for alcohol abuse (Knight et al. 2002), these disorders are largely undiagnosed in student samples. In the experimental chapters of this thesis, any individuals who were diagnosed with substance abuse or dependence were excluded from participating in any studies on ethical grounds. Instead, the AUDIT was used to examine adverse

alcohol related behaviours as well as quantity and frequency of alcohol consumption. The AUDIT was developed by the WHO to assist in brief assessments and identification of risk by categorising drinking behaviour as ‘non-hazardous’, ‘hazardous’ and ‘harmful’, with scores on the AUDIT having been shown to predict likelihood of dependence in various samples (Reinert and Allen 2007).

Heavy drinking during adolescence and early adulthood is considered a risk factor for progression to alcohol dependence in later life (Bonomo et al. 2004; Jennison 2004), whilst also causing significant problems at the time of use. As discussed by the evidence presented in this chapter, it is of the utmost importance to identify what factors contribute to the development and maintenance of alcohol (ab)use among young individuals. If such efforts are undertaken, then it may be possible to intervene before social alcohol use progressively worsens and reaches levels of abuse and dependence, thereby reducing the impact on both the individual and society as a whole. The target population of the research conducted in this thesis were heavy drinkers who had not been diagnosed with alcohol abuse or dependence but were often drinking at harmful levels. This presents an opportunity to examine the behaviours of individuals whose alcohol-behaviours may well progress to become hazardous and problematic over time.

1.3 Addiction characterised as loss of control

The most prominent theories of addiction can be construed in terms of their biological, social or psychosocial processes. The models often deal with one set of these processes or a combination. These candidate processes can then be used to explain addiction in terms of the effects of addictive stimuli, individual susceptibility, environmental factors, recovery and / or relapse (West 2001). Due to the multifaceted and complex nature of addiction there is no unified framework or theory that encapsulates each of these aspects, and as such theories often exist in isolation. Therefore, in order to understand addiction, it is essential to look at these fundamental processes that define or contribute to it.

Addiction, at the individual level, can be seen as a deregulated motivational system in which reward-driven behaviour takes precedence, leading to a loss of control over drug seeking and consumption. This loss of control is evident as one of the main defining criteria of alcohol abuse and dependence according to the DSM-IV, and more than likely, will be evidence for alcohol use disorder under the proposals in the DSM-V discussed above. Defining criteria, such as ‘larger amounts or over a longer period than was intended’ and ‘unsuccessful efforts to cut down or control alcohol use’ are analogies used to define loss of control over behaviour. As such, the most prominent theoretical models of substance (ab)use and addiction implicate this ‘loss of control’ as a major risk factor or consequence at some stage in the addiction/dependence cycle. The following subsections will attempt to demonstrate that various theories exist and implicate this ‘loss of control’ as a feature of addiction through addictive stimuli, individual susceptibility, environmental factors, recovery and relapse. The subsections will review each of these models in detail, and illustrate how these concepts fit in with their predictions by examining the evidence from research using the experimental tasks described below.

1.4 Disinhibition and Response Inhibition

1.4.1 Definition

Disinhibition can be described as the experimental analogue of ‘loss of control’ (Leeman et al. 2009) over volitional and most likely, drug-related behaviour. In terms of alcohol abuse/dependence this can be conceptualised as the inability to resist a drink when already intoxicated or walk past a bar when attempting to abstain. Specifically in regards to this thesis, disinhibition is operationalized as

‘the ability to suppress responses that are no longer required or inappropriate, which supports flexible and goal-directed behaviour in ever-changing environments (Verbruggen and Logan, 2009 pp.648)’.

One of the most common behavioural measures of disinhibition is that of response inhibition - these two terms will be used interchangeably, along with the term inhibitory control throughout.

1.4.2 Measuring Disinhibition: Behavioural Tasks

The stop-signal task

The stop-signal task (Logan and Cowen, 1984) is a widely accepted and established measure of response inhibition. The task usually involves the build up of a pre-potent motor response by requiring participants to categorise stimuli as quickly as possible using a motor response - these are known as 'go' trials. These stimuli can be arbitrary (such as the standard 'x' or 'o' discrimination task), can contain relevant or irrelevant cues (Verbruggen and Logan 2009) or be adapted for use with children by using novel pictorial stimuli (Dimoska et al. 2006). On a minority of trials the categorisation is interrupted by a stop-signal (usually an auditory tone). Individuals are informed that if this stop-signal occurs, they should inhibit their discrimination response. The stop-signal is usually presented at around 25% of trials in order to keep the discrimination response dominant. However, it is common to vary the frequency of stop trials to manipulate response conflict and difficulty of inhibition (Ramautar et al. 2004). The ability to inhibit this dominant response on these 'stop' trials is one measure of inhibitory control.

The stop-signal occurs after presentation of the 'go' stimulus. The delay between the presentations of both stimuli is an important factor of the task. Theoretically, the longer the delay between the two means the more difficult it is to prevent a categorisation response. Different methods of setting the stop-signal delays have been developed in order to tap the full extent of inhibitory processing. The original task used fixed stop-signal delays (Logan and Cowan 1984), other versions include a tracking algorithm (Logan et al. 1997) which adjusts the delays based upon inhibitory performance during the task or delays based on mean reaction time to the go stimulus (Carter et al. 2003).

The task is conceptualised as a race between two competing, independent processes; going and stopping (Band et al. 2003). If the go response is completed before the stopping response, the go response is executed; whereas, if the stopping process finishes first, the go response is inhibited. Under normal circumstances, participants

are instructed to categorize the stimuli as quickly as possible but also to refrain from responding if they hear the stop-signal. In theory, this sets up a response conflict or speed/accuracy trade off, e.g. individuals cannot go too fast or inhibition will undoubtedly suffer, and if they focus on inhibition their reaction times will be slower (Leotti and Wager 2010). An advantage of the stop-signal task is the ability to compute a Stop-signal Reaction Time (SSRT).

SSRT is the epoch from when the stopping process begins (the presentation of the stop-signal) to when it ends, which cannot be directly measured. It is estimated using 'go' reaction times and the probability of successful inhibition, taking into account the response conflict and motivational bias of participants (Leotti and Wager 2010). SSRT is therefore an important measure of inhibitory control, as one's ability to inhibit is influenced by factors such as stop-signal delay and mean reaction time. For example, Schachar and Logan (1990) found that whilst children as young as 8 had similar number of inhibitory errors as older children and adults, their mean reaction times to the stimulus discrimination task were much slower with increased variability, thus making inhibition easier as they were less likely to have initiated their go response. The stop-signal task has been used to measure inhibition in a variety of different psychopathologies as well as healthy controls (for meta-analysis see: Lipszyc and Schachar 2010)

The Go/No-go task

The basic Go/No-go task involves the separate presentation of two different types of stimuli; go cues and no-go cues (Murphy and Garavan 2011). The individual is asked to quickly respond to go cues and not to respond to no-go cues. As with the stop-signal task, dominancy of responding to go cues are usually reinforced by having a greater frequency of go trials. The measure of inhibition in this task is the proportion or number of go responses to no-go cues (known as commission errors).

A common variation is the cued Go/No-go task. This version involves presenting further cues during the task. These cues may provide preliminary information as to the type of stimulus that might appear as the cues have a high probability of signalling the correct stimulus, thus no-go trials preceded by a go cue are the most difficult to inhibit to as individuals are anticipating or actively preparing a motor response (Marczinski and Fillmore 2003; Marczinski and Fillmore 2005). Stimulus

onsets are also varied to keep individuals from anticipating presentation latencies. Cues may also be presented as stimuli i.e. using words or pictures (Houben 2011a, b).

Another variation typically used in substance use research is the passive avoidance task (Newman and Kosson 1986). This task involves four of eight arbitrary numbers being assigned as go stimuli and the remaining four as no-go stimuli. The passive avoidance of the task is usually designed so individuals have to avoid punishment, thus rewards and punishments are often built into these versions of the task to increase participant motivation.

Anti-saccade Task

The anti-saccade task (Hallett 1978) is the measure of inhibition of ocular movements. The most common version of the task involves a small bright target presented in the periphery of a dark screen. There are two types of trials i) pro-saccade trials, which involve the participant making a reflexive saccade towards this target (no response inhibition), and ii) anti-saccade trials, which involve the participant overriding this reflex by making a volitional eye movement in the opposite direction (response inhibition).

Variations in the task include delaying rather than inhibiting a reflexive saccade, known as the delayed ocular return task (Weafer et al. 2011). The anti-saccade task is conceptually different to both stop-signal and Go/No-go tasks (Logan and Irwin 2000), as the anti-saccade task requires the ability to stop or delay an innate process, whereas the motor responding required for stop-signal and Go/No-go tasks is not likely to be innate.

Compared to pro-saccades, anti-saccade trials have more errors, greater variability in fixations and increased reaction times. Compared to behavioural responses, oculomotor responses are much faster (Logan and Irwin 2000). The more errors made and slower reaction times on anti-saccade trials are used in behavioural studies as a measure of (dis)inhibition in clinical and non-clinical populations, including smokers (Powell et al. 2002), drinkers (Roche and King 2010; Weafer et al. 2011) and those suffering from attention deficit hyperactivity disorder (Klein et al. 2003).

Other tasks such as the standard colour conflict Stroop (Rose and Duka 2008) and Hayling tasks (Rose et al. 2010) are sometimes used throughout the literature as measures of (dis)inhibition. However, these tasks are not used with the same frequency as the more common tasks discussed above and as such, will not be discussed at length in this thesis.

Whilst all these tasks are accepted in the addiction literature as measuring the ability to inhibit behaviour there are some fundamental differences between them. Both the stop-signal task and Go/No-go tasks are validated measures of motor inhibition used in the laboratory; however, each may require a different form of inhibition. Schachar et al (2007) argued that the stop-signal task requires ‘action cancellation’ as the stop-signal is presented at a delay, meaning a go response has most likely been initiated. Conversely, in the Go/No go task the decision to inhibit is made upon initial stimulus presentation and thus is deemed ‘action restraint’. Furthermore, Verbruggen and Logan (2008) have suggested response inhibition can become automatic when a stimulus is consistently paired with a stopping response (i.e. the Go/No-go task), yet, in the stop-signal task the presentation of both stop and go signals together makes it difficult for automaticity to develop. Finally, emerging evidence suggests that oculomotor inhibition is different from ‘manual’ or motor inhibition, both structurally and functionally (Roberts et al. 2011), as the anti-saccade task measures inhibition of an innate reflex rather than a pre-potent or habitual response (Logan and Irwin 2000). Therefore, the layout and components of each of these tasks mean there is greater inhibitory pressure in the stop-signal and anti-saccade task, and that a more automatic form of inhibition and decision-making is perhaps more prominent in the Go/No-go task (Eagle et al. 2008). The subtle task differences may play a role in the discrepancies in the developmental and imaging research discussed below.

1.4.3 Development and Neural components

Automatic and impulsive behaviours are considered innate or to develop quickly. On the other hand, executive functioning, specifically inhibition, starts to develop slowly through childhood and continues doing so into adulthood. For example, Tillman,

Thorell, Brocki and Bohlin (2008) investigated the developmental transition of inhibitory performance in a non-clinical sample of 4 – 12 year olds using the stop-signal task (described in section 1.4.3). They found that, cross-sectionally, inhibitory control improved with age suggesting that it is still developing up until the age of 12, at the very least. Furthermore, behavioural studies investigating inhibitory control along with other executive functions show continued development of inhibitory functioning up until age 17 (Anderson et al. 2001) and even into early adulthood (Schachar and Logan 1990; van den Wildenberg and Crone 2006). Throughout early adulthood (ages 19-29), inhibitory control peaks and is at its most efficient before beginning to regress again in later adulthood (age 30+). However, this may be due to the slowing of reaction times rather than deficits in inhibition (Williams et al. 1999).

The relatively slow developmental trajectory of response inhibition is due to the continual maturation of the underlying neural processes that subserve inhibition processes. Human developmental research implicates the development of prefrontal brain regions in the maturation of executive functioning. Behavioural and functional imaging research suggest that during inhibition on Go/No-go tasks (Chapter 1.4.3), children, when compared with adults, show a greater intensity in activation in the prefrontal cortex (Booth et al. 2003; Booth et al. 2004; Casey et al. 1997; Tamm et al. 2002). This increased activation may be due to children applying an increased effort in order to inhibit behaviour. Moreover, there is evidence to suggest response inhibition in adults is acquired through a different neuronal route to children (Rubia et al. 2000). Although contradictory evidence suggests that adults show a greater activation in prefrontal cortex on the stop-signal task (Rubia et al. 2000; Rubia et al. 2007), this is on successful inhibition trials only, further suggesting that the more effort exerted, the greater the likelihood of being able to inhibit behaviour.

Evidence discerning the precise localisation of specific regions that promote inhibition is brought about through lesion and imaging studies. In humans, Aron, Fletcher, Bullmore, Sahakian, and Robbins (2003) compared individuals with lesions to the right Inferior Frontal Cortex (rIFC) to healthy controls and found impaired inhibition suggesting the rIFC as a critical area of inhibition. This finding is supported by functional Magnetic Resonance Imaging (fMRI) studies showing successful inhibitory control correlated with activation in the rIFC (Rubia et al. 2003; Rubia et al. 2007). However, the right inferior pre-frontal cortex is likely to be

one area that is part of a wider circuit of inhibition. Evidence suggests that the rIFC projects the command to inhibit, via the basal ganglia, to the motor coordination areas (Aron et al. 2007). Further imaging evidence suggests activation in the anterior cingulate cortex, sensorimotor cortex and cerebellum (Casey et al. 2000; Rubia et al. 2001) during response inhibition. With regard to the circuitry underlying inhibition, it is worth noting that to inhibit a response is not considered a unitary process (Miyake et al. 2000). Typically, depending on the type of task used, to inhibit a response involves processes such as; conflict detection, attention, memory and motor movement (Booth et al. 2003; Casey et al. 2000). There are indications to suggest that the age at which inhibition peaks is task dependent (discussed in Rubia et al. 2007), as different behavioural tasks have different components and inhibitory pressures (see Chapter 1.4.2).

1.5.1 Impulsivity and Executive Function theories of addiction

Impulsivity has no universally accepted definition; there is considerable diversity in measurement, approach and theory. Early theories, specifically in relation to addiction, described impulsivity only as rash, spontaneous behaviour without thought for consequences. However, Dawe and Loxton (2004) argue that the acquisition and even the use (through preparation), of certain substances, involves considerable goal-directed behaviours and planning. Therefore, they argue that another factor may well be influencing drug-use, in this case 'reward sensitivity'. However, the evidence supporting Dawe and Loxton's two factor approach was drawn mostly from self-report data and personality based questionnaires (such as the Behavioural Activation and Inhibition Scales; Carver and White 1994). Nevertheless, this model was influential in demonstrating the complex nature of impulsivity in relation to motivated or appetitive behaviours.

The idea that impulsivity is a multidimensional construct was further explored by Reynolds et al (2006) using a combination of behavioural measures and self report. Using principle component analysis, they found that both the stop-signal and Go/No-go tasks loaded on the same factor ('impulsive disinhibition'), whereas other

behavioural measures loaded onto a separate factor ('impulsive decision-making'). Furthermore, the behavioural measures were generally unrelated to self reported measures of impulsivity (White et al. 1994). This suggests that the behaviour reportedly measured using self-report questionnaires may not reflect actual behavioural performance. This stands to reason, as behavioural tasks typically only measure one aspect of behaviour (i.e. the stop-signal task measures only disinhibition, whereas the Balloon Analogue Risk Task measures only risk taking; Lejuez et al., 2010), however, questionnaire measures are generally concerned with impulsive behaviour in general. Perhaps the most important difference is that self-reported measures are designed to assess impulsivity as a stable trait, whereas behavioural tasks allow for the assessment of individual differences in impulsivity that may fluctuate over time within individuals.

More recently, the proposed difference between 'disinhibition' and 'decision making' was supported by Christiansen et al (2012b). Using principle component analysis Christiansen and colleagues demonstrated that self reported impulsivity, measured by the Barratt Impulsivity Scale (BIS; Patton et al., 1995) loaded onto a separate factor of impulsive decision making (measured by delay discounting) which in turn loaded on a different factor of disinhibition (measured by Go/No-go performance). Meanwhile, other prominent addiction theories have also supported the multidimensional nature of 'impulsivity' in relation to substance use (de Wit 2009; Dick et al. 2010; Olmstead 2006).

Emerging evidence has begun to relate impulsivity as a direct antipode of executive functioning (Bickel et al. 2012). As previously discussed, executive functioning (or executive cognitive functioning) is a set of general-purpose control mechanisms linked to the prefrontal cortex that exist to regulate behaviour. These behaviours, that also include shifting (between tasks or mental sets) and updating (monitoring and coding incoming information for relevance to the task at hand), are said to show both 'unity' and 'diversity' (Miyake et al. 2000). These functions are often associated with each other ('unity'), which suggests a common underlying ability or process, likely modulated by the pre-frontal cortex. Theories suggest that this underlying ability or process may be working memory, or more specifically, the 'central executive' (Baddeley 1996). The central executive is the structure that is considered responsible for the control and regulation of executive functions. This idea is

supported by Engle and colleagues (Engle 2002; Engle et al. 1999) who suggest a crucial component of working memory is ‘controlled attention’, they argue that any task which involves controlled processing requires ‘controlled attention’ to maintain task relevant information and goals.

Furthermore, recent experimental evidence is beginning to suggest that the three types of behaviours (inhibition, shifting and updating) are subsumed under a common executive function - principally, the ability to maintain task goals and relevant information and use this information to bias lower-level processing. These components are a key requirement for response inhibition (Munakata et al. 2011), thus suggesting that the variance between inhibition and common executive functioning is shared (Miyake and Friedman 2012).

On the other hand, the ‘diversity’ and unique variance of each behaviour has been reported by others, notably, Verdejo-García and Pérez-García (2007). It is important to note that in Miyake and colleagues’ model, the stop-signal task was subsumed under inhibition, whereas Verdejo-García and Pérez-García’s model used a Go/No-go task which was loaded onto the shifting factor, further highlighting the fundamental differences in these tasks (see also Chapter 1.4.2).

Bickel and colleagues (2012) suggest that disinhibition is the antipode of ‘behavioural inhibition’, a component of executive function that refers to three inter-related processes; i) inhibiting an initial pre-potent response; ii) stopping an ongoing response, thereby permitting a delay in the decision to respond; iii) a protection of this period from disruption by competing events. Disinhibition on the other hand is behaviour that is prematurely expressed and likely to result in undesirable consequences, such as succumbing to impulses. The overall rationale for their model suggests that good performance on a stop-signal task maybe interpreted as efficient executive functioning and less impulsive, whereas poor performance may be interpreted as poor executive functioning or an increased impulsiveness. Therefore, impulsivity and executive functioning may exist at opposite ends of the same continuum. Currently there is little apparent overlap between these research areas (Bickel et al., 2012).

Executive function models of addiction suggest automatic, bottom-up human behaviour, such as orientating attention to specific stimuli, mature quickly or are

'hardwired'. These automatic behaviours are advantageous as they can be executed very quickly and they reduce cognitive load for other tasks, however, they are largely inflexible (Miller and Cohen 2001). Tiffany (1990) suggests that as substance use increases it can be initiated automatically. In the context of Tiffany's model of drug use behaviour, once specific drug use behaviours have become automatic they can drive behaviour without full awareness, (e.g. stimulus configurations such as cues will elicit automatic drug seeking behaviour), which may help explain absent minded relapse (Catley et al. 2000). According to Logan (1988), response inhibition is deemed necessary in situations where automatic processes are unavailable or they are no longer the appropriate response. In this case, response inhibition is required to impede an automatic response. Therefore, if these automatic behaviours are impeded, then the individual must employ non-automatic or controlled processing such as response inhibition, to overcome drug urges (Tiffany 1990).

1.5.2 Disinhibition in substance use

There is a large amount of evidence linking disinhibition to substance use cross-sectionally in chronic and dependent users. For example, Fillmore and Rush (2002) examined the performance of chronic cocaine users on both the stop-signal task and Go/No-go against controls, and found that chronic cocaine users had impaired control on both. These deficits were also found in a non-dependent, recreational sample of cocaine use (Colzato et al. 2007). Chronic users of other substances show similar effects, such as Methamphetamine (Monterosso et al. 2005), cigarette smoking (Billieux et al. 2010) and heroin (Fu et al. 2008). Poly-substance users also show inhibitory deficits when compared to a non substance using comparison group (Verdejo-García et al. 2006).

In alcohol dependent individuals, evidence also suggests that response inhibition is impaired compared with controls. In dependent outpatients, psychomotor slowing was found on the stop-signal task, which caused longer SSRTs compared with controls (Lawrence et al. 2009). Similar results were found by Goudraain, Oosterlaan, de Buijs and van den Brink (2006) who found alcoholics, along with

pathological gamblers and those suffering from Tourette's syndrome (disorders of inhibition), performed inferior to controls on a variety of executive function measures including the stop-signal task, Stroop interference and circle tracing. Detoxified alcoholics also made significantly more commission errors on a Go/No-go task using alcohol cues (vs controls) with disinhibition enhanced when alcohol cues signalled a no-go response (Carter et al. 2007). Yet, studies have shown no behavioural differences between controls and alcoholics on a Go/No-go task (Kamarajan et al. 2005a).

In non-dependent users, the cross-sectional findings are less robust. Colder and O'Connor (2002) found commission errors on a passive avoidance Go/No-go task were associated with alcohol use in undergraduate students, and the Go/No-go task has been used to discriminate problem drinkers in college students (Murphy and Garavan 2011), this has been shown to predict unique variance hazardous drinking (Christiansen et al. 2012b). Using questionnaire measures of disinhibition in a sample of university students, Leeman et al (2009) found associations with heavy episodic drinking and alcohol related problems. However, Weafer, Milich and Fillmore (2011) found an association between inhibition failures on a Go/No-go task, but not a variation on the anti-saccade task, with quantity but not frequency of alcohol consumption. Furthermore, Nederkoorn, Baltus, Guerrieri and Wiers (2009b) found heavy drinking females to have impaired response inhibition, but not males, with other studies such as Fernie, Cole, Goudie and Field (2010) failing to show any association between alcohol use and (dis)inhibition in non-dependent samples. Emerging evidence is beginning to suggest that disinhibition in heavy drinkers can also lead to greater increases in craving in response to alcohol cues, compared to heavy drinkers who are less disinhibited, suggesting inhibitory control may also play a role in suppression of craving responses (Papachristou et al. 2012a).

1.5.3 Neuropsychophysiological associations

As well as behavioural evidence, neuropsychophysiological evidence also suggests that brain activity measured by neuronal activation during response inhibition tasks

may also differ in substance users versus controls. Emerging Event Related Potential (ERP) research is beginning to increase understanding of this relationship. ERPs are time-locked, electroencephalographic (EEG) recordings to specific stimuli, allowing for analysis of strength of neuronal activation and also temporal activation in response to the stimuli. The time course of an ERP consists of various components; these components are positive and negative peaks, or neuronal activation and suppression. It is these measurable phenomena which form the bulk of the research into (dis)inhibition. It is suggested that ERP recordings may provide more sensitive indices of disinhibition than behavioural measures (Luijten et al. 2011).

Throughout the literature, the two main ERP components implicated in response inhibition tasks are the frontal N200 (or N2) and the fronto-central P300 (or P3). The letter 'P' meaning a positive peak with 'N' meaning a negative peak or suppression, with the number being the approximate time in milliseconds following the stimulus these fluctuations occur from stimulus onset (Kok et al. 2004). The initial interpretations of these components suggested that because they were larger on trials that involved inhibition; for example stop trials (Kok et al. 2004), no-go trials (Ruchow et al. 2008) and anti-saccades (Wijnen and Ridderinkhof 2009), they reflected a possible inhibition process. However, evidence also suggests that the N200 component is not likely to be involved in the actual motor process of inhibition (Euser and Franken 2012), and research has demonstrated that N200 is larger during unsuccessful rather than successful inhibition (Kok et al., 2004), therefore, the precise function of this component is still under debate.

Research examining the P300 inhibition response is much more robust. In healthy individuals an enhanced P300 response is consistently elicited on various inhibition trials, compared with 'go' trials. Specifically, in the stop-signal task the P300 component amplitude is enhanced on successful rather than unsuccessful stop trials (Dimoska et al. 2006; Kok et al. 2004). In alcoholics and individuals with a positive family history of alcoholism, the P300 response is attenuated during inhibitory control on Go/No-go tasks (Cohen et al. 1997a; b; Kamarajan et al. 2005a; Kamarajan et al. 2005b), suggesting a reduced P300 could be a risk factor for alcoholism. This is further supported by Glenn, Sinha and Parsons (1993) who showed that P300 amplitudes in abstinent alcoholics predicted relapse.

In a non-dependent sample, Oddy and Barry (2009) separated participants using their alcohol consumption into heavy and light drinkers, before administering a Go/No-go task. They found similar effects to studies using alcoholics, in that compared to light drinkers, heavy drinkers showed a globally reduced P300. However, there were no significant differences in behavioural inhibition as was reported by Kamarajan (2005a). This further suggests that the P300 may be a more sensitive measure of disinhibition than behavioural tasks. Unfortunately, there is no existing longitudinal evidence that examines ERPs over a significant period of time, which does not allow for temporal causality to be examined. Evidence does suggest however, that acute alcohol consumption reduces P300 amplitudes on response inhibition tasks compared with placebo (Bartholow et al. 2003; Euser and Franken 2012).

Whilst the associative evidence between disinhibition and substance use is relatively strong, it is difficult to infer the casual role of disinhibition on alcohol consumption from these behavioural or neuropsychophysiological cross-sectional studies.

Individual or group differences in inhibition, at one specific time point, may reflect a stable behavioural pattern; i) that pre-dates drug use, ii) is a consequence of repeated exposure to drugs, or iii) possibly, a direct or indirect effect of drugs (de Wit 2009).

With regards to neuropsychophysiological associations the evidence is similar.

Alcohol use, both in chronic and social drinkers, is associated with reduced P300 (likely a biomarker of inhibition), however, research is yet to examine whether reduced P300 is a cause of alcohol use or a consequence.

There are two hypothesised roles of disinhibition in the association of drug and alcohol use. Either disinhibition is a consequence of long-term plasticity and neurotoxic effects on the brain caused by substance misuse, or disinhibition is a pre-existing risk factor or vulnerability marker that predisposes individuals to substance misuse (Dick et al. 2010; Verdejo-García et al. 2008). One or more of the following theories highlights the direction each of these pathways.

1.6 Neurobiological theories: disinhibition as a consequence of chronic drug use

The neurobiological theories of addiction suggest that the (ab)use of drugs is brought about by the interaction of two systems; what is broadly described as an activation

(or approach) system and an inhibition system. According to contemporary models of addiction, as drug use behaviours escalate into abuse and dependence, individuals develop a bias towards drug-related stimuli. The Incentive Sensitization theory (Robinson and Berridge 1993) suggests that drugs activate and, over prolonged periods, permanently alter the mesolimbic dopamine circuit that influence drug reward effects. These alterations lead to a hyper-sensitive dopamine system. Dopamine attributes salience to cues which increases 'wanting' so cues become hyper salient, leading to an increased motivation to obtain drugs. Furthermore, it is hypothesised that this increased 'wanting' occurs independently of 'liking', as Robinson and Berridge (1993) suggest, drugs lose their affective experience with increased use.

The experimental evidence for the reductionist, neurobiological view of addiction suggests (dis)inhibition is a result of permanent changes in brain structure and function, with evidence consisting mostly of animal models and imaging research. Theories based on animal evidence, such as Jentsch and Taylor (1999), postulate that substance use behaviour is driven by the interaction of the two distinct processes; increased drug saliency (approach) and reduced impulse control (inhibition). Increased drug saliency comes about through repeated drug administration causing sensitization, possibly mediated by the mesolimbic dopamine system as described above. Chronic drug use also causes impairments to frontal cortical regions of the brain; these areas are seen to regulate inhibitory control (see Chapter 1.4.3). Evidence from animal research suggest that both adolescent and adult rodents placed on four day binge ethanol treatment (modelled on human bingeing behaviour) showed significant damage to frontal cortical brain areas, with juvenile rats showing greater sensitivity (Crews et al. 2000). Similar results were found by Nixon and Crews (2002). These neurotoxic effects on the frontal cortices are similar across different drugs of abuse such as cocaine and methamphetamine, administered in binge patterns to animals (Kuczenski et al. 2007). Further evidence also suggests that specific lesions to frontal structures in animals cause disinhibited behaviour (Chudasama et al. 2003).

In human neurobiological models, the pattern of neurotoxicity is very similar. Drugs of abuse not only cause dysfunctions to neurotransmitters such as dopamine and serotonin (Koob and Volkow 2010) leading to increased salience of reward

(Robinson and Berridge 1993), but also cause structural and functional changes to specific brain areas. For example, chronic alcoholics have reduced frontal lobe volumes compared to controls (Pfefferbaum et al. 1997). Kril, Halliday, Svoboda and Cartwright (1997) found similar evidence in that the cerebral cortex was damaged in chronic alcoholics (but not healthy controls) with the majority of neuro-degeneration situated in the frontal lobes. This study demonstrated that damage caused by chronic alcohol use was fairly selective as very little neuro-degeneration was evident in motor response areas. Further studies have found structural loss as a result of long term alcohol consumption (Cardenas et al. 2007; Cardenas et al. 2005), with some evidence to suggest damage to frontal areas is irreversible through long term abstinence (Cardenas et al. 2005). Research has also demonstrated that in a non-clinical sample, only heavy drinkers are at risk for frontal lobe shrinkage in adulthood (Kubota et al. 2001). Finally, there is also emerging evidence to suggest this neurotoxicity is more pronounced in females (Hommer 2003).

Evidence from both human and animal studies suggests that adolescence is a critical period in which the structures governing the approach and inhibition systems are still developing (Crews et al. 2007). As adolescence is also characterised as a period of increased risk taking and reckless behaviour (including drug taking; Steinberg 2008) this suggests that during this period there is increased vulnerability for drugs of abuse to have lasting effects on neurobiological functioning. For example, adolescents who binge drink are more likely to show alcohol induced neurotoxicity (Monti et al. 2005) than non bingers, and individuals who begin drinking in early adolescence are four times more likely to become alcohol dependent in the future (Grant and Dawson 1998).

Goldstein and Volkow (2002) reviewed the neurobiological evidence with their impaired response inhibition and salience attribution syndrome of drug addiction (I-RISA) model. Initially motivation to use substances is driven by increased incentive motivation properties of drugs and related cues (Robinson and Berridge 1993). In normal circumstances motivation to engage in substance use is ruled over by an effective inhibitory control system. However, chronic drug use can cause structural and functional changes that lead to dysfunction in both of these systems. According to the I-RISA model of drug addiction, deficient response inhibition plays a causal role in the relapse and bingeing stages of the addiction cycle. During relapse and

bingeing automatic behaviour takes precedence and must be governed by top-down control. Relapse is, for the most part, due to urges that are not controlled, and bingeing is due to a lack of control over actual consumption.

The common theme that can be drawn from the animal and human neurobiological models is that deficient response inhibition may play an influential role in substance use. Through neurotoxic damage to the frontal lobes response inhibition may be impaired. However, this damage in itself is the result of chronic drug use or bingeing behaviour. Therefore, the evidence base from these models may be appropriate in explaining relapse and bingeing in chronic users. Finally, caution must be exercised when interpreting this evidence, as the majority of human imaging is cross-sectional meaning causality cannot truly be inferred.

1.7 Longitudinal theories: disinhibition as a risk factor.

In order to examine the second possible direction of the relationship between disinhibition and alcohol-seeking, it is of importance to examine whether any pre-existing differences in disinhibition can facilitate the initial uptake and escalation of drug and alcohol use. As the evidence for the role of (dis)inhibition as a possible consequence of chronic drug use is described above, the following section will examine the developmental evidence that (dis)inhibition and poor restraint may be risk factors for substance ab(use) and dependence.

The hypothesis that (dis)inhibition can be a contributing factor is mainly supported by longitudinal studies. In these studies, inhibitory control in childhood and adolescence is used to predict various drug use behaviours and outcomes. In one such study, Wong et al (2006) assessed the developmental trajectory of inhibitory control in a large cohort sample of children of alcoholics and aged matched controls. At specific time points during adolescence, Wong and colleagues found that children who had lower initial levels of inhibitory control (increased disinhibition) and developed inhibitory control at a slower rate (between the ages of 3-14), were more likely to report alcohol-related problems, drink at an earlier age and use other drugs (at ages 14-17) than children with a more rapid inhibitory control development.

Furthermore, these effects were stable when controlling for parental alcoholism. Importantly, the ability to self-regulate behaviour in the form of behavioural resiliency provided some protection against these factors. Similarly, in support of this, evidence from a series of studies by Tarter and colleagues (Tarter et al. 2003; Tarter et al. 2004) investigated the role of 'neurobehavioural disinhibition', a latent variable attained using measures of; executive cognitive functioning, emotion regulation, and inhibitory control. They demonstrated that in boys aged 12, neurobehavioural disinhibition predicted substance use behaviours in later adolescence. This measure of disinhibition discriminated between boys with high and low risk for adolescence but also predicted transition to substance use at age 19.

Further longitudinal evidence comes from a study conducted by Nigg et al (2004), which concentrated broadly on executive cognitive functioning in children of alcoholic parents and controls. The study used the stop-signal task as a measure of (dis)inhibition in early adolescence (aged 12-15), along with tests of response regulation and interference control, in order to ascertain potential risk factors of alcoholism. Children from families with alcohol use disorders (without antisocial behaviour backgrounds) suffered from the greatest impairments in inhibitory control, compared with children from non-alcoholic, antisocial backgrounds, and children from alcoholic and antisocial behaviour backgrounds. Furthermore, the indices of disinhibition in this group were uniquely predictive of their alcohol risk status.

As well as developmental evidence in children, longitudinal evidence in adults has demonstrated similar results. Rubio et al (2008) examined a large group of adults taken from a primary care setting, by giving them a stop-signal task and classifying them according to AUDIT cut-offs. Results showed that in heavy drinkers, levels of disinhibition predicted severity of alcohol dependence at a four year follow-up.

Finally, evidence for poor inhibitory control development and disinhibition predicting substance use disorders, can be drawn from individuals suffering from impulse control disorders such as Attention Deficit Hyperactivity Disorder (ADHD). ADHD is characterised by disinhibited behaviour (Barkley 1997; Nigg 2001) and children who suffer from ADHD often perform poorly on behavioural measures of response inhibition, including the stop-signal task (Schachar and Logan 1990; Schachar et al. 1995), Go/No-go task (Iaboni et al. 1995; Shue and Douglas 1992)

and anti-saccade task (Roberts et al. 2011). There is a large body of evidence that suggests disinhibition is a shared endophenotype for both ADHD and substance (ab)use (Groman et al. 2009). Examining the causality of ADHD suggests that individuals suffering from ADHD in childhood are also at an increased risk for substance misuse in adulthood (Biederman et al. 1998). In support of this, a recent meta-analysis (Lee et al. 2011) suggests children with ADHD are 1.7 times more likely to present with alcohol dependence than controls. Additionally, severity of ADHD symptoms in adulthood predicts quantity of alcohol consumption (Weafer et al. 2011).

Robust evidence suggests an association between (dis)inhibited behaviour during childhood and the subsequent development of substance use disorders. Specifically, in regards to alcohol, numerous longitudinal studies suggest childhood behavioural disinhibition is a vulnerability marker for alcohol consumption in later adolescence. Cumulatively, these studies suggest that pre-existing deficits in inhibition may have a causal influence on alcohol consumption in clinical (ADHD) and non-clinical samples. The evidence from these longitudinal, developmental studies suggests that pre-morbid disinhibition (assessed before exposure to alcohol/drugs) may play a causal role in drug/alcohol-seeking.

1.8 Dual process theories: disinhibition as a possible mediator of the influence of other processes on drug use and abuse

Dual process theories such as Wiers et al's (2007) model of adolescent addictive behaviour are not dissimilar to neurobiological theories. The models also propose excessive alcohol use is the result of an imbalance between two systems; an appetitive system and an executive system (similar to the models of Dawe and Loxton 2004; Goldstein and Volkow 2002). The appetitive system becomes sensitized, with repeat exposure to alcohol or other addictive substances, guiding automatic drug seeking behaviour (Robinson and Berridge 1993). This approach behaviour can be observed both implicitly and explicitly. For example, individuals whom consume greater amounts of alcohol have more positive explicit alcohol

expectancies, and also show greater motivation to consume alcohol (Jones et al. 2001). Increased sensitization of the appetitive system can also lead to an increased attentional bias for substance related stimuli (Field and Cox 2008) and an increased approach-bias (Christiansen et al. 2011).

As with the neurobiological models, this appetitive system can be governed by executive control systems such as inhibitory control. The dual process model of Wiers et al (2007) not only highlights the ability to control behaviour, but also the motivation needed to control it. This is logical as individuals whom consume large amounts of alcohol may have no pre-existing deficits in control but also no motivation to reduce consumption. As this model is specifically focussed on adolescent drinking, as opposed to neurobiological evidence (which is focused on older, chronic users), the control system may well be in a critical period of development to which excessive consumption might impede (Medina et al. 2008).

Wiers and colleagues' (2007) model highlights the need for motivation to regulate behaviours. However, as the model suggests, it is difficult to identify adolescents who realise their drinking may be problematic and therefore be motivated to change this behaviour. The motivation to change behaviour has also been highlighted in a number of treatment models, including motivational interviewing (Miller 1996) and cognitive behavioural therapy (Marlatt 1996), which is more identifiable in a clinical setting. Motivation to change is likely to be low in samples where heavy drinking is considered more normative behaviour (e.g. university students), or where alcohol consumption has yet to cause any major familial/social/physical problems, or led to a clinical diagnosis of abuse/dependence.

The behavioural evidence provides support for the causal role of disinhibition on alcohol use, as a moderator between implicit, approach associations and drinking behaviour. In support of this, Houben and Wiers (2009) measured automatic alcohol pleasant/unpleasant associations using an Implicit Association Task, followed by a measure of response inhibition (colour-conflict Stroop) with a measure of alcohol consumption in social drinkers. The results suggested that, only in individuals who exhibited impaired response inhibition (high Stroop interference scores), drinking behaviour was associated with automatic cognition. This is supported by research into calorie consumption, which demonstrated disinhibited individuals ate in

accordance with their automatic associations towards food (Hofmann et al. 2009). Furthermore, disinhibition as a moderator, rather than a direct cause, has been supported in research on aggressiveness after drinking (Wiers et al. 2009) suggesting those who cannot inhibit behaviour effectively are most aggressive when intoxicated. Whilst the evidence base for the moderating role of disinhibition is in the early stages, it shows promise.

An extension to the dual process model of Wiers and colleagues puts forth the analogy of the 'horse and the rider', with the horse symbolising associative systems e.g. automatic approach and attentional bias, and the rider symbolising executive functioning (Friese et al. 2011). In order to reduce health-risk behaviours (characterised as a smooth horse ride), the focus can be on taming the horse i.e. automatic behaviours. Such methods include attentional bias retraining, which has been shown to reduce immediate alcohol consumption in undergraduates (Field and Eastwood 2005) and also risk of relapse in clinical samples (Schoenmakers et al. 2010), or approach avoidance retraining (Wiers et al. 2010), which has also demonstrated reductions in alcohol consumption. A second focus is strengthening the rider brought about by training executive control systems. In support of this, preliminary research has demonstrated that strengthening working memory reduces alcohol consumption for up to a month, following training (Gladwin et al. 2011; Houben et al. 2011c). Theoretically, this suggests that training inhibitory control may have the same effects. If this were the case, then it would support the hypothesis of a causal relationship between disinhibition and alcohol (ab)use.

To summarise, dual process models suggest that the relationship between alcohol and disinhibition is due to inhibition moderating the relationship between alcohol use and both automatic/implicit and explicit associations. The limited evidence for this theory so far suggests that individuals who show greater disinhibition drink in accordance with their implicit attitudes towards alcohol. The dual process models make two important contributions to our understanding of the relationship between disinhibition and alcohol consumption - i) that motivation to limit drinking may be an important factor, and ii) strengthening implicit cognitions and top-down processes may reduce health-risk behaviours, which is indicative of causality.

1.9 State changes in (dis)inhibition

The research presented above has examined the relationship between disinhibition and substance use, specifically alcohol. Importantly, these relationships have been inferred by assuming disinhibition as a construct, generally stable over time. There is growing evidence to suggest that disinhibition can fluctuate within a short space of time, much like other psychological constructs e.g. mood. Experimental evidence has begun to identify the factors that may promote fluctuations in inhibition. For example, the effects of reward and punishment have been shown to influence response inhibition in a Go/No-go paradigm (Masui and Nomura 2011; Newman and Kosson 1986). Priming response inhibition by using relevant and irrelevant cues has been demonstrated in the stop-signal task by Verbruggen and Logan (2009). Additionally, individual differences in motivational bias have been shown to cause temporary fluctuations in response inhibition (Leotti and Wager 2010).

The evidence presented above has led to a recent review by de Wit (2009) highlighting the need for investigations of factors that may cause fluctuations in disinhibition and whether these fluctuations increase the proclivity for drug use, with the specific hypothesis

“...abrupt environmental, physiological or emotional events (that) may cause transient ‘state’ changes in either self-control or inhibition that may result in re-initiation of drug use’ (p.28)”.

One such model that may inform these investigations is the limited resource model.

1.10 Limited resource models: possible evidence of state fluctuations

The limited resource model of self-control is a move away from the traditional dual process and impulsivity theories as described above that suggest that (dis)inhibition is an enduring, inflexible concept. The model presented suggests that acts of self-control cause short term, or ‘state’ impairments in subsequent self-control. The

original limited resource model, termed the ‘strength model of self-control’, implies self-control as overriding an initial response, thereby making a different response possible which promotes a long term goal (Muraven and Baumeister 2000). This theory makes the analogy that self-control strength is akin to that of a muscle – repeatedly exerting pressure on self-control (or a muscle) reduces strength in the short term for further acts of self-control (or muscle) strength.

This phenomenon of self-control deterioration, termed ‘ego depletion’, is a robust finding throughout behavioural and cognitive literature, demonstrated by a number of original methodologies. For example, Baumeister, Bratslavsky, Muraven and Tice (1998) asked participants to resist the temptation of eating pleasurable foods such as chocolate and cookies (whilst being allowed to eat less pleasurable, ‘healthy’ foods), before presenting them with a frustrating task. The degree of persistence during the task (restraining from quitting the task) was used as a measure of disinhibition/restraint. They found individuals who restrained from the pleasurable foods were more likely to quit than those who restrained from healthy foods or a no food control group. Similar methods of depletion have made people less likely to inhibit aggression (Stucke and Baumeister 2006), or reduce concentration and vigilance (Muraven et al. 2007).

This theory, whilst providing a new perspective that (dis)inhibition and restraint are in fact, not stable over time, may have explanatory potential for why individuals use substances even in the face of negative consequences, or when they have motivation not to. Firstly, resisting the temptation to consume alcohol may reduce subsequent self-control. Muraven and Shmeuli (2006) used cue exposure to deplete resources in social drinkers. They found that individuals who had to resist the urge to drink during exposure to alcohol performed worse on subsequent self-control tasks, than when exposed to water. Secondly, depleted self-control may leave people at risk for subsequent substance use. In smokers, resisting the urge to eat chocolate rather than radishes and broccoli, led to individuals smoking more during a break from the experiment (Shmueli and Prochaska 2009). Muraven, Collins and Neinhuis (2002) depleted self-control resources (using thought suppression) in a group of social drinkers whilst getting a separate group to solve simple, less depleting math problems. They then gave each group *ad-libitum* access to alcohol whilst informing them that post consumption, they would be asked to take a driving simulation task

and that restraining from alcohol on this task would increase their chances of a reward for good performance. The results suggested that even if participants were motivated not to consume (for financial reward), initial self-control depletion increased *ad-libitum* alcohol consumption. Further evidence for increased alcohol-seeking behaviour when restraint would be the better option comes from studies by Ostafin et al, (2008) and Christiansen et al (2012a). Ostafin and colleagues demonstrated that when self-control resources are depleted, automatic motivations to drink are strongly related to alcohol consumption, thus supporting both self-control as a regulatory system and Wiers and colleagues dual process model (2007). However, Ostafin and colleagues inferred self-control dysregulation (without measuring it) and when Christiansen and colleagues did measure it using a Go/No-go task, disinhibition did not mediate *ad-libitum* consumption after ego depletion.

Recently, the analogy of self-control as a muscle has been extended further, with research suggesting that self-control can be trained (similar to the theory of training executive functions described above). The training of self-control will, theoretically, increase self-control strength (similar to increasing muscle size), thus attenuating the depleting effects of exerting control. With regards to motivated behaviours, such as alcohol-seeking and smoking, evidence suggests this seems to be the case. For example, individuals who practiced self-control, in the form of reducing sweet consumption or squeezing a handgrip, over a two week period, demonstrated a greater ability to control behaviour on a stop-signal task, relative to baseline performance. Indirect self-control training, such as the uptake and maintenance of an exercise programme, also led to increased control over a wide range of regulatory tasks in the lab, but also extended to decreases in smoking, alcohol consumption and caffeine, independent of changes in perceived self-efficacy and stress outside of the laboratory (Oaten and Cheng 2006). In those motivated to restrain behaviour similar effects have been found. Individuals wanting to quit smoking had lower relapse rates when training their self-control two weeks prior to giving up (Muraven 2010).

To summarise, the limited resource models may overlap somewhat with the dual process models, but also offer a unique explanation of disinhibition. The understanding that (dis)inhibition and restraint, in the form of self-control, can fluctuate throughout individuals over time has explanatory potential for excessive consumption and relapse in situations of depletion. The evidence that self-control

can be improved, similarly proposed in the horse and rider model (Friese et al. 2011), may also prove an area of research that may inform treatment and prevention outcomes. However, the model has limitations, not only as an explanation for substance use, but overall. The model is yet to be tested in clinical samples such as alcoholics, and studies rarely take into account other traits that may influence alcohol-seeking, such as craving, pre-existing self-control capacity, etc. Furthermore, depleted self-control (which is supposedly akin to disinhibited behaviour) is often inferred in novel and unempirical ways, such as length of time squeezing a handgrip. A meta-analysis on the convergent validity of these tasks suggests that self-control is multifaceted (Duckworth and Kern 2011). Finally, the definition of self-control is under debate and may be characteristically distinct from (dis)inhibition (Fujita 2011). Therefore, it needs to be addressed whether these methods translate to poor performance as measured by more validated response inhibition tasks, such as the stop-signal and Go/No-go tasks.

As well as methodological issues that impact the model in terms of explaining addiction processes, the mechanisms driving 'ego depletion' effects are not well understood. It may be that effects are moderated by perceptions of depletion. In a series of studies, Clarkson et al (2010) attenuated the ego-depletion effect by providing false feedback about perceived mental resources. That is to say individuals who were ego depleted performed similarly to 'non-depleted' individuals on self-control task when they believed a depletion task increased their self-control resources. Similarly, individuals who were led to believe that they have unlimited self-control resources do not show ego depletion effects (Job et al. 2010; Vohs et al. 2012). Finally, ego depletion effects have also been extinguished through financial motivation (Baumeister et al. 2005), suggesting beliefs and motivations may play an important role in actual, or perceived, self-control.

1.11 Acute alcohol consumption and disinhibition

As well as the long term effects of chronic drug use, acute alcohol intoxication may also lead to disinhibited 'states' which reflect the more irreversible changes in

disinhibition caused by chronic use. The 'priming' effect of alcohol, in which consumption of alcohol leads to the desire to drink more, may be, in part, due to the disinhibitory effects alcohol has on behaviour (Rose and Duka 2008). For example, under moderate and heavy doses of alcohol (0.4 – 0.65 grams of alcohol per kilogram of body weight) individual's inhibitory control on both stop-signal and Go/No-go task is consistently impaired (Field et al. 2010).

The sensitivity of impairment under intoxication is associated with *ad-libitum* alcohol consumption. Weafer and Fillmore (2008) gave individuals a dose of 0.65g/kg of alcohol (vs placebo) and found that inhibitory performance was impaired. After the acute intoxication, participants were given *ad-libitum* access to alcohol under the guise of a bogus taste test. They found that the magnitude of disinhibition caused by the initial dose of alcohol explained a large amount of variance in subsequent alcohol-seeking behaviour. Individual differences, such as gender, may moderate the effects of alcohol pre-loads on inhibition. Fillmore and Weafer (2004) gave a moderate dose of alcohol (0.6g/kg) and placebo to a group of males and females and found only males showed any significant impairment in inhibition.

The mechanism of this 'state' disinhibition may be due to alcohol's acute effects on the frontal lobe. A recent study by Tsujii, Sakatani, Nakashima, Igarashi and Katayama (2011) used near-infrared spectroscopy after priming individuals with 0.5g/kg of alcohol and a placebo. This technique measures cortical hemodynamic responses to stimuli, with an increased blood flow indicative of neural activation. The results suggested that the alcohol prime increased commission errors, and a negative association between rIFC activation and commission error rates. This suggests that those who show greatest disruption of brain activation through acute alcohol effects, exhibit larger deficits in disinhibition. This unique study examines alcohol's acute effects directly on frontal lobe functioning and suggests that acute alcohol may have the same effect, albeit temporary, as chronic alcohol consumption.

In conclusion it is evident that acute alcohol consumption can lead to disinhibited behaviour. The evidence from within subject studies suggests that these impairments are short term, (compared to placebo), suggesting the effects are due to the pharmacology of alcohol. Furthermore, the evidence suggests that individual

sensitivity to the 'state' disinhibition caused by the alcohol prime may be a risk factor of increased consumption or bingeing. Finally, it is apparent that the acute affects of alcohol consumption on brain functioning mirror the effects of chronic consumption, suggesting alcohol selectively impairs certain brain areas associated with inhibition.

1.12 Motivations and Beliefs: Drinking restraint

As both the dual process and limited resource models imply that beliefs and restraint are important factors which may influence disinhibition and alcohol consumption, this thesis will attempt to investigate these constructs. Relatively little research has been performed on this topic in non-dependent samples, even though the ability to exercise restraint is conceptually different from the *belief* in one's ability to exercise restraint, and ones *motivation* to restrain.

However, in dependent samples one such model that examines the possible role of beliefs in substance use is that of self efficacy (Rollnick and Heather 1982). Self-efficacy is the individual's belief they can exhibit coping behaviours in a high risk situation. Self-efficacy theory has had some success in predicting relapse in smokers (Ockene et al. 2000), but not alcoholics (Burling et al. 1989; Miller et al. 1996), however, the magnitude of effects on smoking are negligible (Gwaltney et al. 2009) and the mechanisms of the relationship between the two are not well known (Maisto et al. 2000) . Furthermore, as discussed, the construct of self-efficacy is only really applied to clinical samples.

A similar concept, which is more applicable to non-dependent samples, is that of drinking restraint. Drinking restraint is the combination of two separate constructs; 'high desire to drink' and 'concurrent attempts to control this drinking' (MacKillop et al. 2006a) (p.157). Paradoxical to the behavioural evidence that effective inhibitory control may be protective against excessive consumption, motivation to restrain is often associated with excessive consumption in non-clinical samples, such as college students (Collins et al. 2001). Specifically, in non-dependent samples, the high desire to drink, measured by the Temptation and Restraint Inventory's

Cognitive Emotional Pre-occupation subscale (described in Chapter 2.1) is considered a proximal predictor of drinking in college students (Lyvers et al. 2010; Williams and Ricciardelli 1999).

One model that attempts to explain this paradox is the Limit Violation Effect (Collins and Lapp 1991). This model suggests non-dependent drinkers who have high drinking restraint impose limits on their alcohol intake - these limits may be situational or stable in order to achieve a longer-term goal. However, if a proposed limit is broken it may lead to excessive drinking behaviour to counteract negative mood. The mechanism behind this is the attribution of fault. Collins and colleagues suggest that if individuals attribute the Limit Violation internally, e.g. a belief they could not control drinking, this leads to increased negative affect. The prediction of this theory is that an increased negative affect should lead to increased drinking in order to attenuate feelings of negative mood. Evidence does suggest that individuals exhibiting high levels of drinking restraint impose limits and that breaking these limits causes an increase in negative mood (Collins and Lapp 1991; Muraven et al. 2005a)

The relationship between drinking restraint, negative mood and drinking in this model is uncertain. Laboratory studies failed to find the association, and actually found the opposite effect in that increased negative mood leads to a reduction in drinking (Collins 1993; Collins et al. 1994). However, in the case of this model, studies using Ecological Momentary Assessment are likely to be more informative as temporal patterns are more indicative of causality. Muraven and colleagues (Muraven et al. 2005a; b) tested the assumptions of the limit violation effect on social drinkers over two weeks. The findings supported the hypothesis that violation of an imposed limit increased distress, which exacerbated subsequent drinking, with heavy drinkers showing greater sensitivity to predicted limit violation effects.

A more recent theory, which examined the effects of restraint as a belief, is that of Nordgren et al's (2009) 'Restraint Bias'. According to the Restraint Bias theory, the belief that one can overcome temptation through self-control may actually lead to disinhibited behaviour in the form of increased exposure to temptation. Nordgren and colleagues (2009) tested these predictions in a series of experimental and naturalistic studies that tested individuals' restraint beliefs against motivated

behaviours, such as smoking and food snacking. The findings suggested that either by direct manipulation, such as feedback, or indirect manipulation via hot state induction (craving), individuals over estimated their self-control leading to an increased exposure to temptation and an increased uptake of motivated behaviours. These innovative findings supported their hypothesis that self-control beliefs can cause disinhibited behaviour, characterised as an increased exposure to temptation and substance use. They may also explain individual differences in drinking restraint beliefs on substance use behaviour, in social, rather than dependent users. According to Nordgren and colleagues, the predictions set forth by ‘Restraint Bias’ also have the potential to explain relapse in abstinent users. For example, once physical withdrawal and craving are diminished by detoxification, individuals will begin to overestimate their self-control, ultimately leading to disinhibited behaviour and relapse.

The theories about beliefs and motivations are often examined in isolation, and rarely discussed in association with research on disinhibition as impaired control over behaviour. However, as the dual process model suggests, individuals with efficient inhibitory control may exercise it when they are motivated to do so. As behaviour, motivations and beliefs all seem to be associated with alcohol consumption, theoretically, it is important examine their effects.

1.13 Interim summary

So far this thesis has discussed the major psychological theories that propose disinhibition is in some way associated with substance (ab)use. Whilst each model proposes a role for disinhibition, or a breakdown in self-control/restraint at some point in a cycle or progression of substance use, the function is generally not consistent across models meaning the causal relationship is difficult to infer. There are few possible reasons for this; i) the model only focuses on one particular aspect of drug use, ii) the construct of disinhibition may have more than one role, or iii) the model focuses on a specific population. Reviewing the evidence from the above mentioned theories might ascertain that all of these explanations are accurate.

With regards to the neurobiological models of drug use the structural brain changes that cause deficits in executive functioning, specifically inhibition, are brought about through long term, chronic alcohol use (Goldstein and Volkow 2002; Lyvers 2000). Therefore, the applicability to adolescent and young adult social drinkers, for example, the majority of university students, may be limited as the magnitude of structural neurotoxicity develops over many years of hazardous drinking. Furthermore, these theories often neglect the initial determinants of substance (ab)use. If the initial feature influencing chronic consumption is pre-morbid disinhibition, then although the relevant areas are damaged, the inability to control behaviour still preceded drug/alcohol use.

The evidence from the developmental and dual process models may shed some light onto initial alcohol consumption. These models suggest a break down in inhibitory control or a pre-existing deficit increases individuals vulnerability for substance (ab)use (Nigg et al. 2006; Nigg et al. 2004; Wong et al. 2006), possibly through the inability to regulate/control implicit approach mechanisms. An important contribution from the dual process theories (Wiers et al., 2007) is the emphasis on motivation and beliefs. Whilst these models are more applicable to adolescent alcohol use, a potential drawback is that they discuss inhibition/restraint solely in terms as a trait variable, stable over time or developing slowly over adolescence, with the exception of the limited resource models.

Whilst the advantage of the limited resource models is that it suggests that disinhibition can fluctuate throughout individuals dependent on a limited pool of self-control, it is not specifically a model of addiction, therefore, many prominent factors that influence drug seeking (i.e. craving, impulsivity) are not examined in these studies. Also there is some evidence suggesting the effect may not be driven by actual self-control, rather by the belief that one has been depleted. If we examine the effects of acute intoxication causing alcohol consumption, the evidence is more conclusive. Acute alcohol consumption reliably induces an increase in disinhibition. The next logical step in investigating causality is to examine whether, at any given time, state fluctuations in disinhibition can influence drug consumption within sober individuals (the above mentioned hypothesis of de Wit (2009)). This hypothesis has yet to be fully investigated. However, recently emerging evidence has begun to examine the first part of the hypothesis, suggesting that

‘...abrupt environmental, physiological or emotional events (that) may cause transient ‘state’ changes in either self-control or inhibition...’

in dependent or non-dependent samples using the validated measures of disinhibition discussed above (Chapter 1.4.2).

1.14 Experimental evidence of transient disinhibition in drug using populations

With regards to substance using individuals, stress imagery has been shown to increase disinhibition in smokers (vs non smokers) relative to baseline (Schepis et al. 2011). Exposure to alcohol cues in detoxified alcoholics showed increases in SSRT compared with exposure to neutral cues (Gauggel et al. 2010). Furthermore, acute stress has been shown to augment the effects of alcohol cues on disinhibition, specifically in male problem drinkers (Zack et al. 2011). This evidence suggests that inhibition is influenced by current motivations and environmental factors (e.g. ability to obtain reward, control urges, exposure to stress), and can indeed fluctuate throughout individuals over short periods of time.

In response to this, research has begun to directly influence disinhibition and restraint, and examine the effects on motivated behaviours. In an original study Guerrieri et al., (2009) manipulated participant instructions on a stop-signal task; prompting one group to respond with restraint (‘inhibition group’) by placing a motivational emphasis on inhibition, and another group to respond with disinhibition (‘impulsivity group’) by placing emphasis on reaction times. These instructions led to differential performance by groups on the stop-signal task; the group required to respond with restraint demonstrated slower reaction times but fewer inhibition errors, and the disinhibited group showed increased reaction times but more inhibition errors, suggesting fluctuations in behaviour. Furthermore, during subsequent *ad-libitum* calorie consumption, those who were in the disinhibited group consumed more calories.

In an attempt to provide the first experimental evidence that examined effusively de Wit’s (2009) hypothesis, I adopted Guerrieri et al’s (2009) methodology in a

research project published prior to this thesis (see Jones et al. 2011a). In a sample of social drinkers, the same methodology caused the same effects on group behaviour as the original study – increased disinhibition vs increased restraint – but also group differences in *ad-libitum* alcohol consumption, measured using a bogus taste test (see Chapter 2.2). Individuals, who received the instructions placing emphasis on speeded responses at the expense of inhibition, drank a significantly higher percentage of non-alcoholic beer (disguised as alcoholic) than those primed to respond with an emphasis on inhibition. Furthermore, I demonstrated that in individuals who were primed to respond with restraint, performance on the stop-signal task was associated with their subsequent beer consumption. That is, the less disinhibited they were, the less alcohol they consumed. This was, to my knowledge, the first experimental evidence that state fluctuations in disinhibition can cause alcohol-seeking in sober individuals, whilst also supporting individual difference observations in alcohol prime studies (Weafer and Fillmore 2008).

1.15 Hypothesis and Aims

On the basis of previous research (Jones et al. 2011a; Guerrieri et al. 2009), the overall aim of this thesis was to examine the hypothesis that disinhibition can fluctuate, and whether any fluctuations influence alcohol-seeking in heavy drinkers. By focusing on this hypothesis we can attempt to provide some of the first experimental evidence that disinhibition can cause alcohol-seeking in sober, non-dependent individuals. The importance of identifying the causality of disinhibition is twofold – firstly, to provide support and increase our understanding of theoretical models of addiction, and secondly, if causality is established, then treatments for addiction may focus on increasing inhibitory control or inoculating individuals against fluctuations in disinhibition.

As well as examining the overall effects of disinhibited states on alcohol-seeking, this thesis will also examine any possible mechanisms which may drive the effects, such as craving or mood/arousal, both of which have been shown to influence the motivation to consume alcohol. Furthermore, in an attempt to integrate personality

factors, such as impulsivity and motivation to restrain, outlined in the models above, self-report measures of each were taken in all experiments.

Chapter Three focused on replicating and extending the initial findings of Jones et al. (2011a), and attempted to clarify any possible mechanisms that influence alcohol-seeking. A comparison group was included in order to examine which set of instructions led to changes in behaviour and alcohol-seeking.

Chapter Four then sought to examine whether these specific instructions caused not only behavioural differences, but also neuropsychophysiological differences in measures of disinhibition. Additionally, I examined whether neuropsychophysiological (Event Related Potential) components were associated with behavioural measures and *ad-libitum* alcohol consumption.

Chapter Five attempted to examine whether inhibition can be trained, specifically for alcohol related cues. In addition, I examined whether training inhibition towards alcohol cues caused a reduction in alcohol-seeking in the laboratory, and whether the effect persisted at a week long follow-up (Experiment One). Finally, I examined whether these potential causal relationships translated to a different form of inhibition, specifically oculomotor inhibition (Experiment Two).

In Chapter Six, I examined the role of alcohol cues on disinhibition and alcohol-seeking, by testing de Wit's (2009) hypothesis (that environmental cues might influence disinhibition) in a semi-naturalistic setting (a simulated bar environment). The distinction between this chapter and previous is that I did not directly manipulate disinhibition using emphasis on a particular response or a modified task, but rather examined whether the indirect effects of olfactory alcohol cues increased disinhibition.

In the final experimental chapter (Chapter Seven), I set out to provide the first empirical evidence that suggests beliefs about disinhibition can also fluctuate and those restraint beliefs, as well as behaviour, may be important predictors of *ad-libitum* alcohol consumption.

Chapter Two

General Methods

2.1 Questionnaires.

Multiple baseline measures were taken at the beginning of each study. The majority of these measures were consistent across all six studies, as a result the format of each are described in detail only once in this instance. The detail and rationale for each of the multiple baseline measures are described below, as well as their psychometric properties.

Two Week Timeline Follow-back (TLFB; Sobell and Sobell 1992).

The TLFB was used at the beginning of each experiment to assess fortnightly alcohol consumption in UK units. The TLFB involves individuals retrospectively determining their alcohol consumption on a day-to-day basis for the preceding two weeks, up until the night before the experimental session. In this case, a unit guide specifying the number of units in most common alcoholic drinks was provided with the TLFB (e.g. single pub measure of vodka (37.5 ABV) = one unit). Participants were allowed to consult diaries and/or mobile phones to help aid their recall.

The TLFB has been used successfully as a relatively quick way to gauge quantity and frequency of alcohol consumption in both problem drinkers, but also social drinkers. The paper and pencil version of the TLFB was used as research suggests that data obtained from this measure is as reliable as interview methods (Hoeppe et al. 2010). The TLFB is often used to examine drinking patterns over a longer period of time, such as the traditional 30-day diary (Henges and Marczinski 2012) or even up to 12 months (Sobell and Sobell 1992). However, completion rates and accuracy for such long recalls can be low in social drinkers (Hoeppe et al. 2010). In this

case, the two week version was used as research suggests that shorter recall is more accurate and a long enough time to capture typical drinking patterns.

The test-retest reliability of shorter TLFBs (≤ 4 weeks) is generally quite high in both dependent and non-dependent samples with correlation coefficients ranging from .75 to $> .90$ in some cases (Cohen and Vinson 1995; Sobell et al. 1986) .

Alcohol Use Disorders Identification Test (AUDIT; Saunders et al. 1993)

The AUDIT was administered, in questionnaire form, in order to further assess quantity and frequency of alcohol consumption, but also to examine behavioural problems associated with alcohol consumption. The AUDIT is a ten-item scale with the first three questions related to quantity and frequency of use. These questions can be used in isolation as a short form of the questionnaire (AUDIT-C). The last seven questions tap into behaviours associated with drinking and consequences of drinking (such as memory loss, injury). Each of the ten items is scored from 0 – 4 giving the AUDIT a possible score of 40. Various cut-offs are used in order to establish drinking behaviour and/or level of risk. According to WHO guidelines, scores of ≥ 8 are indicative of hazardous or harmful use, with a risk of dependence. A score of ≥ 20 warrants further diagnosis to examine alcohol dependence. Further cut offs can be used to determine the magnitude of risk and type of intervention, for example, a score between 8 and 16 represents medium risk of alcohol problems with simple advice recommended as an intervention. Finally, cut offs can be altered to increase/decrease specificity and sensitivity, depending on national and cultural standards.

As a measurement tool, the AUDIT has been found to be robust with a high degree of internal consistency. Reinert and Allen (2007) examined 18 studies using the AUDIT and found a median reliability coefficient of .83, with a range of .75 to .97. Furthermore, it has also been shown to have a high test-retest reliability (Dybek et al. 2006) . The specificity/sensitivity of the AUDIT is comparable to, and often exceeds other alcohol screening methods (Allen et al. 2001), thus proving it an effective tool to measure problem drinking and associated risk status.

Temptation and Restraint Inventory (TRI; Collins and Lapp 1992)

As Wiers and colleagues (2007) suggest, motivation may be an important factor limiting alcohol use, therefore it was decided to measure self reported motivation to limit alcohol use. The TRI is a self-report Likert style questionnaire consisting of 15 items that assess cognitive restraint, and motivation to reduce drinking. The 15 items load onto two factors, the Cognitive Emotion Preoccupation (CEP) and the Cognitive Behavioural Control (CBC) subscale. These two factors moderately correlate with each other and relate to distinct constructs. The CBC measures the degree in which restraint to alcohol is deemed successful, whereas the CEP measures unsuccessful attempts at regulating drinking. When taken together they measure the 'individual's propensity to engage or resist in drinking' (p.630). Both the CEP and CBC subscales have been demonstrated to predict unique variance in weekly consumption (Collins and Lapp 1992). More recent studies have shown the TRI predicted alcohol consumption and risk of dependence in adolescent drinking samples (Williams and Ricciardelli 1999).

The two-factor structure of the TRI has been validated in clinical samples of alcohol dependent inpatients with good internal consistency. Psychometric validation has also been done in hazardous college drinking samples (MacKillop et al. 2006b) with robust internal validity estimates of .87 for the whole scale, with .85 and .83 for the CEP and CBC subscales respectively.

Barratt Impulsivity Scale version 11 (BIS; Patton et al. 1995).

The BIS provides a self-reported measure of trait impulsivity. The 30 statements in this case are scored from 1-4 using the anchors 'rarely', 'occasionally', 'often' and 'always'. The BIS is made up of three subscales; Motor Impulsiveness, Attention and Non Planning, using total scores on each. A BIS total score can be computed by adding scores on the three subscales to give an overall measure of impulsiveness.

The internal consistency of the BIS has been demonstrated with undergraduates (.82), substance abuse patients (.79) and general psychiatric patients (.83). Test-retest scores are robust, as is criterion validity (Patton et al. 1995; Stanford et al. 2009). However, internal consistencies of the subscales are varied (Motor Impulsiveness .59; Attentional; .74 Non Planning .72).

Approach and Avoidance of Alcohol Questionnaire (AAAQ; McEvoy et al. 2004)

The AAAQ was used throughout the thesis as a measure of self-reported craving. The questionnaire has 14 statements, scored from 0 (not at all) to 8 (very strong), that load onto three unique subscales, measuring three dimensions; mild inclinations to drink (Inclined / Indulgent), intense inclinations to drink (Obsessed / Compelled) and inclinations to avoid alcohol (Resolved / Regulated). Mean scores from the items in each subscale are used. The subscales have been shown to predict a large amount of variance in the quantity (53%) and frequency (49%) of alcohol consumption in Australian samples, and similar proportions explained (41% and 60%, respectively) in an American sample. Scores on each of the three subscales have been shown to distinguish risk status in college drinkers, with high risk drinkers scoring higher on the Obsessed subscale, and no-risk drinkers scoring higher on the resolved subscale. The internal consistencies were as follows; Inclined .89, Obsessed .84, Resolved .63, with similar results shown in alcohol-dependent patients (Klein et al. 2007). As craving was assessed before and after each experimental manipulation (except for Chapters Four and Six, in which it was only measured following the manipulation), the “right now” version of the AAAQ was used to assess any immediate changes.

Brief Mood Introspection Scale (BMIS; Mayer and Gaschke 1988).

The BMIS is a list of 16 adjectives each with a 4-point scale anchored by ‘definitely do not feel’, ‘do not feel’, ‘slightly feel’, and ‘definitely feel’. These adjectives load onto four continuums; pleasant-unpleasant, arousal-calm, positive-tired, and negative-relaxed. Cronbach’s alpha reliabilities are generally good for each continuum, ranging from .76 to .83. Again, in all studies a ‘right now’ version was used to assess any immediate changes.

Post-task feedback questions.

In order to gauge participants’ attitudes towards experimental tasks used, a post-task feedback questionnaire was developed. Based on a similar version used by Muraven and Slessereva (2003), participants were asked how frustrating, irritating, difficult etc, the task was from 1 to 7 with two anchors specifying the extremes e.g. ‘not at all’ and ‘extremely’.

Funnelled debriefing (Field et al., 2007).

A funnelled debriefing was also used in all studies to assess for demand characteristics. It consisted first of an open ended question, ‘What was the purpose of this experiment?’ to which participants were asked to write a short paragraph. Following this a series statements were presented including, ‘The computer task was designed to...?’ and ‘The purpose of the taste test was to...?’; each had between 5 and 8 possible answers, with one being correct.

2.2 Bogus taste test / *ad-libitum* alcohol session

Alcohol-seeking behaviour was inferred in each study using an *ad-libitum* consumption session disguised as a taste test. Whilst the overall procedure for each study was the same there were some differences (in volume given, drink brand, flavour) between each. Therefore, the overall procedure will be described but specific details will be given in each chapter.

The taste-test paradigm was originally developed by Marlatt, Demming and Reid (1973) in which non-abstinent alcoholics were given 15 minutes to taste and rate an alcoholic and non-alcoholic beverage on a large amount of adjectives from a memory drum. The paradigm was later refined by Field and Eastwood (2005) for social drinkers by reducing the amount of alcohol involved and limiting the number of adjectives to four, with participants choosing when they had drunk enough.

At the beginning of each *ad-libitum* session, participants were given equal amount of beer and fruit juice and asked to rate them on a scale of 0 (not at all) to 10 (extremely) on 10 set adjectives (the same for both beverages). Numbers of adjectives were increased in order to improve the face validity. Importantly, participants were explicitly told they could drink as much or as little as they wanted in order to make their judgements. The dependent measure of the taste-test is beer as a percentage of total fluid consumed. This measure is preferable to raw beer consumption in millilitres for various reasons. Firstly, using this method allows for direct comparability with animal literature on taste preference. A second reason was to ensure consistency with other human experimental studies (Field et al. 2007; Field and Eastwood 2005; Jones et al. 2011a). Finally, by using beer as a percentage of

total fluid it takes into account individual differences in thirst, but also how each individual responds to the task. For example, some participants tend to sip both drinks whereas others consume the majority of both drinks - this leads to very high standard deviations and outliers if raw consumption data is analysed. Additionally, in an extension to previous laboratory studies, the pleasantness rating of each drink was assessed in order to ensure this did not influence *ad-libitum* consumption above and beyond any of the experimental manipulations.

Chapter Three

Priming a restrained mental set reduces alcohol-seeking independently of mood.

This experiment was designed as an extension to my previously published study (Jones et al., 2011a). Whilst the previous study had an interesting proof of principle design it had several limitations, and this experiment was designed in order to address these.

This chapter was published as an original report in *Psychopharmacology* (2011: Vol: 218(3) pages 557-65). The peer review process requested I split all independent variables by gender to make it accessible for future meta-analyses and also to include raw consumption scores (as online supplementary materials). Throughout the rest of the thesis it is referred to as Jones et al. (2011b). The format, but not content, has been changed to be consistent with the rest of the thesis.

The roles of the other three authors of the paper version in regards to publication are summarized below:

I designed the study, which was approved by Matt Field (primary supervisor). I collected and analysed the data. I wrote the manuscript. Matt Field, Andrew Goudie (at the time was a secondary supervisor) and Jon Cole (member of research group) gave comments on the manuscript before submission and following peer review.

3.1 Abstract

Rationale: Cross-sectional research demonstrates that heavy drinking is associated with elevated impulsivity, including disinhibition. However, causal effects of disinhibition on drinking behaviour are not well established.

Objective: To experimentally manipulate disinhibited versus restrained mental sets before exploring their impact on alcohol-seeking behaviour, and to investigate if any effects of the manipulation occurred independently of arousal, mood, and craving.

Methods: The study utilized a between-subjects design in which participants were randomly allocated to experimental groups. Social drinkers (N=90) attended the laboratory for a single session where they initially completed a stop-signal task. Different mental sets were induced by emphasising either the importance of cautious responding and successful inhibition (Restraint group), the importance of rapid responding (Disinhibition group), or the equal importance of rapid responding and successful inhibition (Control group). Heart rate, blood pressure, and subjective mood were assessed, before participants completed a bogus taste test procedure.

Results: The Restraint group consumed less beer than the Disinhibition and Control groups, which did not differ from each other. There were no group differences in heart rate, blood pressure, or self-reported mood after the manipulation. Across the whole sample, cautious responding during the stop-signal task (slower reaction time to 'Go' cues, fewer inhibition errors) was associated with reduced beer consumption.

Conclusions: These findings suggest that temporary fluctuations in disinhibited/restrained states may play a causal role in drinking behaviour.

3.2 Introduction

‘Impulsivity’ is a collective term for a range of behaviours that are rash, poorly planned, or that focus on short-term outcomes at the expense of negative long-term consequences (Dawe and Loxton, 2004). Specific behaviours include: risk taking, delay discounting (the preference for a small reward available immediately instead of a larger reward available after a delay), and disinhibition (the inability to withhold an inappropriate response) (Reynolds et al. 2006). While all of these behaviours fall under the umbrella term ‘impulsivity’, they are considered unique and unrelated (Dick et al. 2010). Each of these components of impulsivity is reliably associated with substance misuse and addiction (Verdejo-García et al. 2008).

Disinhibition, or the inability to inhibit a pre-potent response is one of the most widely accepted and well researched components of impulsivity (Logan et al. 1997). The (in)ability to inhibit action is a prominent feature of (poor) self-control, often seen as the nexus of disorders such as attention deficit disorder (Nigg 1999; Slaats-Willemse et al. 2003) and substance misuse (Wills et al. 2006). Response inhibition can be measured by simple tasks such as the stop-signal task (Logan and Cowan 1984) and the Go/No-go task (Marczinski and Fillmore 2003). These tasks require participants to respond rapidly to one (usually visual) stimulus but also to inhibit their response on a minority of trials when a different stimulus is presented. For example, during the stop-signal task, a visual ‘Go’ stimulus is presented, and participants must respond to this stimulus as quickly as possible. On about 25% of trials, an auditory ‘Stop’ stimulus is presented some time after onset of the Go stimulus, and participants must inhibit their response whenever they hear the tone. The task sets up a ‘race’ between the speed of responding and the speed of response inhibition, with the ‘winner’ dictating whether the participant is able to inhibit their response or not (Band et al. 2003).

Evidence suggests a relationship between disinhibition and substance misuse disorders, including alcohol problems. For example studies that used the Go/No-go and stop-signal tasks highlight a deficit in inhibitory control in alcohol dependent individuals compared to controls (Goudriaan et al. 2006). Some recent studies suggest that this aspect of impulsivity is associated with drinking habits even in non-

dependent drinkers, with heavier drinkers having worse inhibitory control. However, this association may be specific to female participants (Nederkoorn et al. 2009), and it has not always been shown in non-dependent drinkers (Fernie et al. 2010).

It is impossible to infer cause and effect relationships from cross-sectional studies such as these: individuals with poor inhibitory control may be more vulnerable to heavy drinking and alcohol use disorders (Nigg et al. 2006; Wong et al. 2010; Wong et al. 2006), or chronic heavy drinking may lead to damage to the prefrontal cortex, with disinhibition as a behavioural consequence (Goldstein and Volkow 2002). To complicate the matter further it is possible that any relationship that exists between the two is mediated by other variables, such as reward sensitivity (Perry and Carroll 2008).

The tendency to act impulsively appears to fluctuate within individuals, in response to variables such as environmental context and the presence of tempting cues (Gauget al. 2010; Wingrove and Bond 1997). Further evidence for state fluctuations in impulsive responding comes from a recent study in which it was demonstrated that the rate of disinhibited responding could be influenced by reward or feedback. In other words, disinhibited behaviour was dependent on the current value that individuals placed on successful inhibition (Leotti and Wager 2010). With regard to substance use, de Wit (2009) discusses “abrupt environmental, physiological or emotional events (that) may cause transient ‘state’ changes in either self-control or inhibition that may result in re-initiation of drug use” (p28). If impulsivity is indeed a ‘state’, then experimental manipulations of this state could prove a very useful tool for exploring the causal role of disinhibition on drinking behaviour and other motivated behaviours.

In a recent study, we (Jones et al. 2011a) adapted a methodology described by Guerrieri et al. (2009) to prime a disinhibited or a restrained mental set in a group of social drinkers, before examining the effects on alcohol-seeking behaviour. We primed different mental sets in our participants by instructing them to either focus on successful inhibition (Restraint group) or rapid responding (Disinhibition group) as they completed a stop-signal task. We found that the Restraint group subsequently consumed less beer during a bogus taste test, compared to the Disinhibition group. We also found that, in our Restraint group, the volume of beer consumed was

associated with cautious and restrained responding during the stop-signal task (i.e. slower go reaction time and fewer inhibition errors). Comparable results were reported in a recent study by (Houben et al. 2011a), who found that social drinkers who received training to improve their response inhibition in the presence of alcohol-related cues consumed less alcohol than a comparison group who were trained to respond rapidly, and were not required to inhibit their responding, when alcohol-related cues were presented. Both of these studies demonstrate that disinhibited/restrained states can be temporarily induced, and that these states have a causal influence on alcohol-seeking behaviour.

In the present study, we used an improved methodology in an attempt to replicate and extend our previous findings. Firstly, we added a control group, which enabled us to clarify the nature of the earlier findings (Jones et al. 2011a). Specifically, the inclusion of a control group allowed us to investigate if task instructions which place the emphasis on behavioural disinhibition would lead to increased alcohol-seeking (relative to the Control manipulation), or if task instructions which place the emphasis on cautious responding, with successful inhibition, would lead to reduced alcohol-seeking (relative to the Control manipulation), or if both processes would be in operation. We also included measures of physiological arousal (heart rate and blood pressure) and self-reported mood, in order to rule out the possibility that increased consumption in the Disinhibition group was influenced by negative mood (Litt et al. 1990; Willner et al. 1998) due to failed inhibitions in this group.

Our first hypothesis was that the differential task instructions would lead to group differences in stop-signal task performance, as they did in our previous study (Jones et al. 2011a). Secondly, we hypothesised that the groups would differ in beer consumption during a bogus taste test, with the Disinhibition group consuming the most and the Restraint group consuming the least. Finally, we predicted that beer consumption would be correlated with indices of stop task performance: those participants who responded more slowly to go cues, and who made fewer inhibition errors, would drink less beer.

3.3 Method

Participants

Ninety social drinkers (40 male, 50 female) were recruited by advertisements placed within the University of Liverpool. Participants who responded to the advertisement were initially screened via email to ensure that they met the inclusion and exclusion criteria (self-reported consumption of alcohol at least once per week, with no history of alcohol use disorders). No participants were excluded on the basis of initial screening. The mean age of the sample was 20.4 (SD=2.9) years. All participants provided informed consent before taking part in the study, which was approved by the University of Liverpool Research Ethics Committee.

Materials and Equipment

Blood pressure and heart rate monitoring: Participants' diastolic and systolic blood pressure and heart rate were measured using a digital blood pressure cuff (Digital Automatic Blood Pressure Monitor M7: Omron Healthcare Europe Ltd, Milton Keynes, UK).

Stop-signal task: We used a version of the task with fixed stop-signal delays (Logan and Cowan 1984). The task was programmed using Inquisit 2.0 (Millisecond Software, 2002), and was presented on a 15inch monitor. The stop-signal (auditory tone) was presented via headphones. Each trial began with a white fixation cross in the centre of the screen presented for 500ms, immediately followed by presentation of a 'Go' stimulus (the letter 'X' or the letter 'O'), for 1000ms. Participants were required to rapidly categorise the stimulus by pressing the correspondingly labelled key on the computer keyboard. Go stimuli were uninterrupted on 75% of trials. On the remaining 25% of trials, an auditory stop-signal was presented at a delay of either 50, 150, 250, or 350ms after the onset of the Go stimulus. Participants were instructed to inhibit responses to the Go stimulus whenever they heard the stop-signal (but see Procedure section, below). The task was split into four blocks; an initial training block of 16 trials (12 Go trials and four Stop trials, one at each delay), which contained feedback on correct and incorrect responses. Participants then completed three blocks of 64 trials, each containing 48 Go trials and 16 Stop trials, with each stop-signal delay occurring four times per block. Trials were presented in a

new random order on each block, and response accuracy and latency were recorded. The primary dependent measure from the task was the number of failed inhibitions on stop-signal trials.

Procedure

Participants were informed that the study was an investigation of the relationship between reaction time and taste perception of different drinks. All testing took place within the Human Psychopharmacology Laboratories in the School of Psychology between 12pm and 6pm. After providing informed consent participants provided a breath alcohol sample; all participants had a zero reading. They then completed a retrospective timeline follow-back diary (Sobell and Sobell 1992) to obtain an estimate of average weekly alcohol consumption. Participants also completed a battery of questionnaires comprising the Alcohol Use Disorders Identification Test (AUDIT) (Saunders et al. 1993), the Temptation and Restraint Inventory (TRI) (Collins and Lapp 1992), and the Barratt Impulsivity Scale, version 11 (Patton et al. 1995). Self-reported alcohol craving and subjective mood were then assessed with the 'right now' version of the Approach and Avoidance of Alcohol Questionnaire (AAAQ) (McEvoy et al. 2004), and the Brief Mood Introspection Scale (BMIS) (Mayer and Gaschke 1988), respectively. Heart rate and blood pressure were then recorded, a procedure which took around one minute.

Participants then completed the stop-signal task. Participants were randomly allocated to 'Restraint', 'Disinhibition', or Control groups; group allocation was balanced across gender. All participants were given the same basic instructions on how to complete the task: they should respond quickly to the go stimuli and inhibit responding whenever they heard the tone. However, for participants in the Restraint group, the importance of successful inhibitions was emphasised, with rapid responding of less importance. For participants in the Disinhibition group, the importance of rapid responding was emphasised, with successful inhibitions less important. The control group were informed that both rapid responding and successful inhibition were equally important. All participants then completed an identical version of the stop-signal task, which took around 12 minutes to complete. Immediately after completion of the stop-signal task, further heart rate and blood pressure readings were taken, before participants completed another AAAQ and BMIS. Participants also answered six further questions concerning their impressions

of the task (based on Muraven and Slessareva (2003)) (e.g. ‘how frustrating was the task’?, ‘how difficult was the task’?), which were answered using a 7 point Likert scale. Participants were then given a chilled 275ml bottle of Becks beer (5.0% ABV) and a chilled 275ml bottle of ‘J²O’ apple and melon flavoured fruit juice. They were asked to rate each drink on 10 different dimensions (e.g. gassy, pleasant, light) using 10 point Likert scales. They were presented with both drinks simultaneously and explicitly informed that they could drink as much or as little of each drink as they wished in order to complete the rating scales. After participants had finished rating the drinks, bottles were removed and the total volume of each drink consumed was measured. This taste test procedure (or slight variants thereof) is sensitive to experimental manipulations of the motivation to drink and it provides an ecologically valid assessment of alcohol-seeking (Field et al. 2007; Field and Eastwood 2005; Jones et al. 2011a).

Finally, participants completed a funnelled debriefing questionnaire, which allowed us to assess their awareness of the aims and hypotheses of the study. After completion of this questionnaire, participants were thoroughly debriefed before receiving either course credit or £5 as financial compensation for their travel expenses and their time. The experiment took around forty-five minutes to complete.

3.4 Results

Group characteristics (see Table 3.1)

Differences between groups were investigated using a series of One Way Analyses of Variance (ANOVAs) with post-hoc Least Significant Difference (LSD) comparisons where necessary. Participant age and scores on the Attentional Impulsiveness subscale of the BIS were log transformed before analysis to improve their distributions. There was a significant group difference on the Cognitive and Emotional Preoccupation subscale of the Temptation and Restraint Inventory [TRI CEP] ($F(2, 89) = 3.17, p < .05$). The Restraint group had higher scores on this subscale compared to the other two groups ($p < .05$), who did not differ from each other ($p > .1$). Groups did not differ on any other variables. As a consequence of this

group difference, scores on TRI CEP were included as a covariate in all subsequent analyses.

Stop-signal task performance (see Table 3.2)

Group differences in performance on the stop-signal task were analysed using Univariate Analysis of Covariance (ANCOVA), with post-hoc LSD comparisons as appropriate. Scores on TRI CEP were added as a covariate. Inhibition Errors and Go Errors were log transformed before analysis to improve their distributions. There were significant group differences in the number of Inhibition Errors ($F(2, 86) = 98.72, p < .01$), the number of Go Errors ($F(2, 86) = 23.20, p < .01$), and Go Reaction time ($F(2, 86) = 54.34, p < .01$). The Disinhibition group made significantly more Inhibition Errors than the Control group, who in turn made significantly more Inhibition Errors than the Restraint group ($p < .01$). The Disinhibition group also made significantly more Go Errors than Control and Restraint groups ($p < .01$), although the latter two groups did not differ from each other ($p > .1$). Finally, the Disinhibition group were quicker to respond to Go cues compared to the Control group, who were in turn quicker than the Restraint group ($p < .01$). The correlation between TRI CEP and inhibition errors was not statistically significant ($r = -.047, p > .1$). These data indicate that the experimental manipulation was successful, as the Restraint group responded more slowly and more cautiously (and so made fewer Inhibition Errors) than the Disinhibition group, with performance of the Control group falling in between these groups. We also calculated stop-signal reaction time (SSRT) using the integration method (Logan and Cowan, 1984), but these data are not presented as the large group differences in go reaction time mean that SSRTs are not directly comparable between groups.

Taste test (see Figure 3.1)

Group differences in beer consumption (as a percentage of total fluid consumed) were analysed using a Univariate ANCOVA, with post-hoc LSD comparisons as appropriate. Scores on TRI CEP were added as a covariate. The main effect of Group was statistically significant ($F(2, 86) = 6.30, p < .01$). Participants in the Restraint group consumed less beer than participants in the Disinhibition ($p < .01$) and Control groups ($p < .05$), although Disinhibition and Control groups did not differ from each other ($p > .1$).

Data from the taste test were re-analysed with the addition of gender as a further between-subjects factor. The Gender x Group interaction was not statistically significant ($F(2, 83) = 0.56, p > .1$). Therefore, there were no differential effects of the experimental manipulation on beer consumption during the taste test in Male and Female participants.

Pleasantness ratings for both beer and juice were analysed using Univariate ANCOVAs. There was no significant difference between groups for either juice ($F(2,87) = .59, p > .1$) or beer ($F(2,87) = .06, p > .1$) pleasantness ratings, suggesting the perceived pleasantness of the drinks played no role in beer preference. Total volume of fluid consumed did not differ significantly between groups ($F(2,87) = .87, p > .1$), neither did total juice consumption ($F(2,86) = .40, p > .1$), suggesting that the manipulation did not increase overall consumption or juice consumption specifically, i.e. effects were specific to beer consumption.

Blood pressure, heart rate, self-reported craving and mood, and post-task feedback (Tables 3.3 and 3.4)

Systolic blood pressure, diastolic blood pressure and heart rate were analysed using mixed design ANCOVAs, with a within-subjects factor of time (2: before stop-signal task, after task) and a between-subjects factor of Group. Scores on TRI-CEP were added as a covariate. There were no significant main effects of Group, Time, or Group X Time interactions for any of these variables ($F_s < 2.47, p_s > .09$).

Therefore, the experimental manipulation had no effect on these physiological measures.

Scores on the AAAQ were log transformed before analysis to reduce skewness. These data were then analysed using a mixed design ANCOVA, with within-subject factors of AAAQ subscale (3: Inclined-Indulgent, Obsessed-Compelled, Resolved-Regulated) and Time (2: before stop-signal task, after task), and a between-subjects factor of Group. Scores on TRI-CEP were added as a covariate. Most importantly, neither the interaction between Group and Time ($F(2, 86) = 0.90, p > .1$), or the three way interaction Group X Time X AAAQ subscale ($F(4, 172) = 0.51, p > .1$) were statistically significant, suggesting no effect of the experimental manipulation on alcohol craving. There were, however, significant main effects of AAAQ subscale ($F(2, 172) = 26.65, p < .01$; scores on the Inclined-Indulgent subscale were higher

than scores on the other two subscales), time ($F(1, 86) = 7.94, p < .01$; overall, craving tended to decrease over time), and Group ($F(2, 86) = 3.51, p < .05$; overall, craving was higher in the Restraint group).

BMIS data were analysed using a mixed design ANOVA, with within-subjects factors of BMIS subscales (4) and Time (2: before stop-signal task, after task) and a between-subjects factor of Group. Scores on TRI-CEP were added as a covariate. Importantly, the interactions between Group and Time ($F(2, 83) = 0.40, p > .1$), and the three way interaction Group X Time X BMIS subscale ($F(6, 164) = 0.31, p > .1$) were not statistically significant, suggesting no effect of the experimental manipulation on self-reported mood.

Finally, participants' self-reports of their impressions of the task (obtained only once, after completion of the stop-signal task) were analysed using a Multivariate Analysis of Covariance (MANCOVA), with a between-subjects factor of group and TRI CEP as a covariate. This revealed a marginally significant multivariate main effect of Group ($F(12, 164) = 1.79, p = 0.05$). Looking at individual items, there were no between group differences in ratings for 'frustration', 'pleasant', 'fighting urge', 'annoyed', or 'irritating' ($F_s < 2.33, p_s > .1$). However, there was a significant group effect for ratings of 'difficult' ($F(2, 86) = 11.01, p < .01$). Post hoc LSD comparisons revealed that the Restraint group found the task less difficult than both the Disinhibition and Control groups ($p_s < .05$), although Disinhibition and Control groups did not differ from each other ($p > .1$).

Given this group difference in the perceived difficulty of the stop-signal task, we re-analysed the taste test data, as described above, but with the addition of difficulty ratings as a further covariate. The main effect of Group remained highly statistically significant ($F(2, 85) = 6.44, p < .01$), and there was no effect of difficulty ratings ($F(1, 85) = 0.50, p > .1$). Therefore, perceived difficulty of the stop-signal task did not appear to influence beer consumption during the taste test.

Supplementary analyses: Participant awareness

Based on responses to the post-experimental funnelled debriefing questionnaire, participants were categorised as aware or unaware of (1) the purpose of the stop-signal task (i.e. to encourage participants to respond more or less 'impulsively'), (2)

the purpose of the taste test (i.e. to measure how much beer participants would drink), and (3) the overall purpose of the study (to influence beer consumption by encouraging participants to respond more or less impulsively during the stop-signal task). Only two participants were classed as aware of the overall purpose of the study; when those participants were removed before reanalysing the taste test data, the main effect of group remained statistically significant ($F(2, 84) = 6.49, p < .01$). Six participants were aware of the purpose of the stop-signal task, but their removal did not affect the result from the taste test either ($F(2, 80) = 6.45, p < .01$). Twenty-nine participants were aware of the purpose of the taste test. The percentage of participants who were aware of the purpose of the taste test did not differ between experimental groups (Control 31%, Disinhibition 43%, Restrained 24%; ($\chi^2 = .66, p > .1$)). Rather than remove these participants from the analysis, we added taste test awareness as an additional between subjects factor before repeating the taste test analysis. The main effect of group remained statistically significant ($F(2, 83) = 3.82, p < .05$) but the group x taste test awareness interaction was not statistically significant ($F(2, 83) = .66, p > .1$). Overall, these results show that participant awareness of the purpose of the study was limited and it did not influence the primary result, i.e. the effects of the experimental manipulation on beer consumption during the taste test.

Supplementary analyses: Associations between performance on the stop-signal task and beer consumption

Associations between beer consumption during the taste test procedure and our three indices of stop-signal task performance (reaction time to Go cues, number of errors on Go trials, number of Inhibition errors) were investigated using Pearson correlations (one-tailed). Across the whole sample, beer consumption was negatively correlated with reaction time to Go cues ($r = -.24, p < .05$), positively correlated with the number of Inhibition errors ($r = .26, p < .01$), and there was a trend for a positive correlation with the number of errors on Go trials ($r = .16, p = .07$). Overall, participants who responded more slowly and cautiously (and therefore made fewer Inhibition errors) tended to consume less beer.

3.5 Discussion

Participants who were instructed to respond with restraint during a stop-signal task subsequently consumed less beer than participants who had been instructed to respond rapidly (rather than cautiously), and participants in a control condition who received standard instructions which emphasised both rapid responding and successful inhibition during the task. These results replicate and extend our earlier findings (Jones et al. 2011a), and they suggest that the effects of our experimental manipulation cannot be attributed to arousal, subjective mood or craving, or demand effects. Overall, these results demonstrate that instructing participants to respond with restraint while performing a stop-signal task seems to induce a restrained mental set which carries over to influence alcohol-seeking behaviour when assessed subsequently with a bogus taste test procedure.

The use of a more detailed methodology than the previous study (Jones et al. 2011a) allows us to explicate our previous findings, as well as those of Houben et al. (2011a). As we noted in our earlier report, interpretation of the results is difficult because it could indicate that induction of a 'disinhibited' mental set increased alcohol-seeking behaviour, or induction of a restrained mental set decreased alcohol-seeking behaviour. Indeed, both processes may have been in operation. The present results suggest that, because the control group consumed more beer than the restrained group but did not differ from the disinhibited group, priming a restrained mental set during a stop-signal task leads to a reduction in subsequent alcohol-seeking behaviour. Priming a disinhibited mental set does not increase alcohol-seeking behaviour more than a control manipulation, in which rapid responding and successful inhibitions are emphasised as equally important. These results support the results discussed by Houben et al. (2011a), and consideration of all three studies suggests that training participants to improve their response inhibition may reduce alcohol consumption. However, future studies of this type may wish to consider using an experimental manipulation which generates a more potent disinhibited mental set, for example by completely removing the instruction to inhibit responding for participants in the Disinhibition group, in order to examine if a disinhibited mental set can increase alcohol-seeking relative to a control manipulation.

These results have a number of important theoretical and clinical implications. Our findings add to those reported by (Jones et al. 2011a) to suggest that a restrained vs. disinhibited mental set can influence response inhibition and alcohol-seeking behaviour. This is important support for theoretical models which argue that individual differences in the ability to inhibit behaviour are an important determinant of loss of control over drug-seeking behaviour in substance use disorders (Dawe and Loxton 2004; Goldstein and Volkow 2002; Jentsch and Taylor 1999). Our manipulation of task instructions may mimic individual differences in response biases during response inhibition tasks (Leotti and Wager 2010). To extend this analogy and consider its implications for alcohol consumption, individuals who regularly exercise restraint may find it easier to limit their alcohol consumption than individuals who place less emphasis on restraint. The parallel literature on ego depletion suggests that training self-control may mitigate against effects of depleted self-control resources (Baumeister 2003; Hagger et al. 2010; Muraven and Baumeister 2000), which provides further support for this explanation.

Future research could explore any potential clinical applications of this novel finding, and try to identify the underlying mechanisms that drive this effect. For example, repeated induction of a restrained mental set may lead to long term improvements in response inhibition, or provide greater resistance to any behaviour that depletes self control resources (Baumeister 2003), leading to concomitant reductions in drinking behaviour over longer periods of time (Houben et al. 2011a). Emerging research suggests that pharmacotherapy can have therapeutic benefits on impulse control disorders such as ADHD and substance abuse (Chamberlain et al. 2009), and these agents may work by improving behavioural flexibility. The priming of a restrained mental set as reported here may be a non-pharmacological alternative that ultimately works through similar mechanisms.

In addition to adding a control group, we also modified our methodology in order to examine if the hypothesised effects of our experimental manipulation on beer consumption could be attributed to physiological arousal, negative mood, or alcohol craving, rather than changes in response inhibition. Importantly, there were no between-group differences in physiological measures of arousal (heart rate and blood pressure), or in self-reported mood. While the restraint group did perceive the stop-signal task as less 'difficult' than the other two groups, this seems an unlikely

explanation for group differences in beer consumption, because these effects remained statistically significant even when self-report ratings of task difficulty were statistically controlled. Attribution of the group differences in beer consumption to the restrained mental set that was induced by task instructions is supported by the correlations that were reported, which show that beer consumption was associated with the degree of behavioural restraint during the stop-signal task (participants who responded more slowly and who made fewer inhibition errors, consumed less beer).

While a minority of participants appeared to be aware of the true purpose of the stop-signal task (to encourage a disinhibited or a restrained mental set) and / or the bogus taste test (to measure the motivation to drink beer), demand effects do not seem a plausible explanation for the reported results, because exclusion of participants who were aware of the true purpose of these tasks did not influence the reported results. Finally, as in our previous study (Jones et al., 2011a), the experimental groups did not differ in self-reported alcohol craving after completing the stop-signal task, so beer consumption appears to have been influenced in the total absence of altered subjective states (see above discussion of mood). These findings point to the dissociation between subjective craving and drug-seeking behaviour (see Tiffany 1990; Wiers et al. 2007) and are consistent with results from other cognitive manipulations which demonstrate that alcohol-seeking in the laboratory can be influenced independently of subjective craving (e.g. Wiers, Rinck, Kordts, Houben, and Strack (2010)).

Finally, we note some potential limitations of the study that should be considered when interpreting the results. Firstly, there were pre-existing group differences on the cognitive and emotional preoccupation subscale of the TRI. This variable was statistically controlled in all analyses, which suggests that group differences in stop-signal task performance and beer consumption can be attributed to the experimental manipulation rather than to group differences on the TRI. Nonetheless, future studies should attempt to ensure that experimental groups do not differ on drinking-related variables before taking part in any experimental procedures. Secondly, one could argue that the task instructions provided to the disinhibited group mean that this group are not placed into a powerful disinhibited mental set, as they are still required to inhibit whenever possible, despite the emphasis on rapid responding. This may account for the lack of group differences in beer consumption between the

disinhibited and control groups. Future studies should consider induction of a disinhibited mental set, with no requirement for inhibition at all, in order to investigate this issue. Finally, it was not possible to investigate effects of the experimental manipulation on stop-signal reaction time (SSRT), given the large variance in reaction time distributions across groups, so our data do not reveal if our experimental manipulation influences the speed of stopping processes.

In summary, the present results suggest that social drinkers who are primed to respond with restraint before completing a stop-signal task subsequently drink less beer during a bogus taste test compared to a group who are primed to respond rapidly and without restraint, or a control group for whom rapid responding and successful inhibitions are equally important. These effects occurred independently of subjective mood or craving, and the pattern of correlations suggests that the degree to which participants complied with instructions (i.e. to respond more rapidly and less cautiously, or vice versa) was associated with their subsequent beer consumption. These results add to a growing body of evidence which suggests that improving response inhibition can lead to a reduction in drinking behaviour

Table 3.1 Characteristics of participants allocated to Control, Disinhibition and Restraint groups.. Values are means (standard deviations in brackets)

	Control (N=29)	Disinhibition (N=30)	Restraint (N=31)	<i>F</i> (2, 89)	<i>p</i>
Gender Ratio	13 : 16	13 : 17	14 : 17	-	-
Age (years)	19.86 (1.51)	20.97 (3.80)	20.39 (2.80)	1.09	.34
Alcohol consumption	46.66 (23.03)	50.43 (35.01)	49.13 (29.45)	0.12	.88
AUDIT	13.86 (5.54)	13.30 (4.98)	15.77 (5.26)	1.86	.16
BIS Attention	19.76 (2.71)	18.97 (3.06)	19.61 (3.02)	0.73	.48
BIS Motor	25.45 (4.73)	25.70 (5.40)	24.77 (5.00)	0.27	.76
BIS Non Planning	28.28 (6.26)	27.70 (6.24)	28.45 (4.91)	0.14	.87
TRI CEP	21.14 (7.16)	21.87 (8.49)	26.35 (10.22)	3.17	.05*
TRI CBC	14.14 (6.45)	16.10 (8.31)	17.61 (7.96)	1.5	.22

Alcohol consumption = average self-reported weekly alcohol consumption in UK units (1 UK unit = 10ml or 8g of pure alcohol); AUDIT = Alcohol Use Disorders Identification Test; BIS = Barratt Impulsivity Scales; TRI = Temptation and Restraint Inventory, CEP = Cognitive and Emotional Preoccupation, CBC = Cognitive Behavioural Control.

Table 3.2 Performance on the stop-signal task, shown separately for Control, Disinhibition, and Restraint groups. Values are covariate adjusted means (standard error in brackets)

	Control	Disinhibition	Restraint
Reaction time to 'Go' cues (ms)	590 (21)	433 (21)	742 (21)
Number of errors on 'Go' trials	0.79 (0.37)	3.67 (0.36)	0.81 (0.36)
Number of Inhibition Errors	7.58 (1.47)	34.41 (1.44)	2.78 (1.44)

Both 'Inhibition' and 'Go' errors expressed as the mean number of total errors across the three experimental blocks. 'Go' reaction time is expressed as the mean reaction time on successful go trials across the three experimental blocks. Data from the practice block not analysed.

Table 3.3 Heart rate, blood pressure, self-reported mood and alcohol craving, shown separately for Control, Disinhibition, and Restraint groups, before and after completion of the stop-signal task. Values are covariate adjusted means (standard error in brackets)

	Pre-Manipulation			Post-Manipulation		
	Control	Disinhibition	Restraint	Control	Disinhibition	Restraint
Heart Rate (bpm)	74.83 (2.59)	75.33 (2.53)	71.90 (2.54)	72.84 (2.36)	75.97 (2.30)	70.96 (2.31)
Systolic BP	121.44 (3.31)	111.83 (3.24)	114.70 (3.24)	107.70 (3.74)	109.93 (3.66)	110.05 (3.67)
Diastolic BP	71.61 (2.07)	71.77 (2.02)	70.45 (2.0)	70.47 (2.36)	70.87 (2.31)	70.84 (2.31)
BMIS Pleasant	9.10 (1.01)	10.24 (0.96)	7.39 (0.95)	8.82 (1.20)	9.06 (1.15)	6.06 (1.13)
BMIS Arousal	13.86 (0.70)	15.20 (0.67)	15.13 (0.66)	13.43 (0.61)	14.24 (0.58)	14.38 (0.58)
BMIS Negative	3.77(0.45)	4.04 (0.43)	5.04 (0.43)	3.60 (0.46)	3.99 (0.44)	5.23 (0.44)
BMIS Positive	8.04 (0.67)	8.91 (0.67)	7.96 (0.63)	7.73 (0.69)	8.06 (0.66)	6.95 (0.65)
AAAQ Obsessed	0.59 (0.21)	0.79 (0.20)	1.21 (0.20)	0.55 (0.17)	0.99 (0.67)	1.17 (0.16)
AAAQ Inclined	4.51 (0.35)	4.26 (0.34)	4.73 (0.33)	4.31 (0.36)	4.01 (0.34)	4.53 (0.34)
AAAQ Resolved	0.96 (0.22)	0.79 (0.20)	1.49 (0.21)	0.84 (0.22)	0.69 (0.21)	1.24 (0.20)

Bmp = beats per minute; BP = blood pressure; BMIS = Brief Mood Introspection Scale; AAAQ = Approach and Avoidance of Alcohol Questionnaire.

Table 3.4 Participant responses to the stop-signal task. Values are covariate adjusted means (standard error in brackets)

	Control	Disinhibition	Restraint
Frustrating	3.39 (0.34)	3.03 (0.33)	3.21 (0.34)
Pleasant	1.93 (0.31)	1.49 (0.30)	2.43 (0.30)
Fighting an urge	2.28 (0.35)	1.98 (0.34)	2.47 (0.34)
Annoyed	1.99 (0.33)	2.03 (0.33)	2.37 (0.33)
Difficult	2.11 (0.27)	1.86 (0.26)	0.93 (0.26)
Irritating	2.67 (0.32)	2.93 (0.31)	2.99 (0.31)

Items were presented in a 7 point Likert scale, anchors were ‘not at all’ (1) and ‘extremely’ (7).

Figure 3.1 Beer consumption (as a percentage of total fluid consumed) among participants in Control, Disinhibition, and Restraint Groups. Values are covariate adjusted means \pm SEM

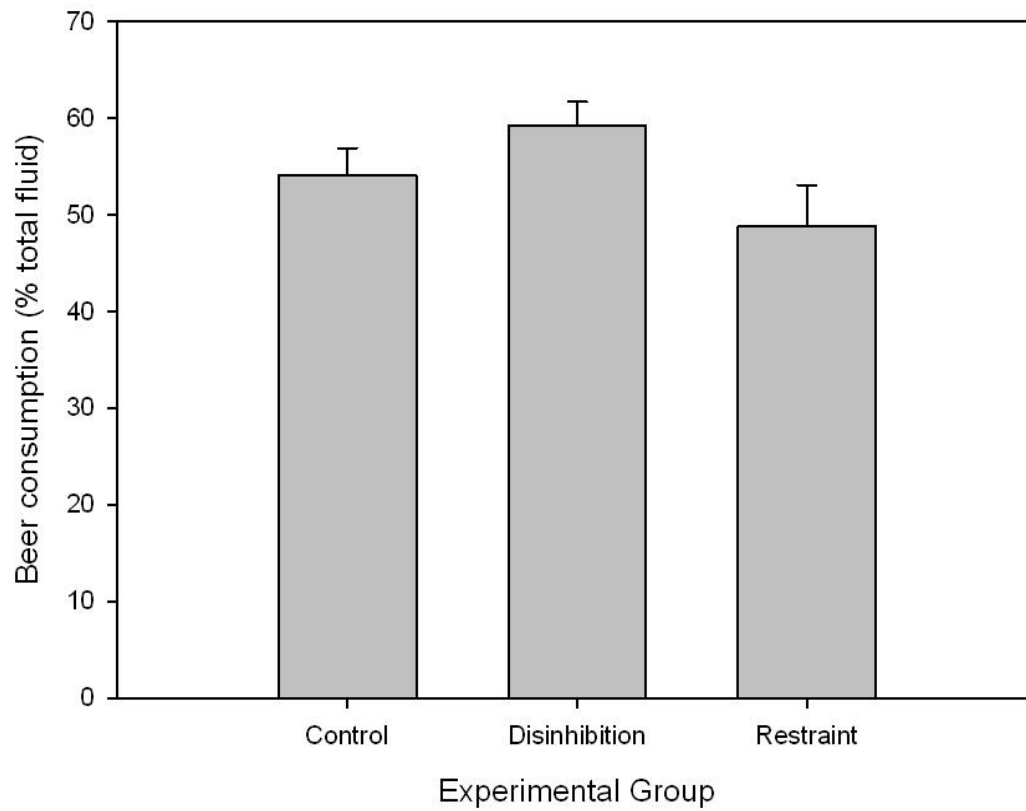


Table 3.S.1 Characteristics of participants allocated to Control, Disinhibition and Restraint groups, split by gender. Values are means (standard deviations in brackets)

	Control (N=29)		Disinhibition (N=30)		Restraint (N=31)	
	Male	Female	Male	Female	Male	Female
Gender Ratio	13	16	13	17	14	17
Age (years)	19.85 (1.86)	19.88 (1.20)	20.85 (2.85)	21.06 (4.48)	20.71 (3.77)	20.12 (1.73)
Alcohol consumption	55.31 (25.39)	39.63 (18.89)	58.46 (46.82)	44.29 (22.03)	56.00 (32.55)	43.47 (26.27)
AUDIT	13.54 (4.79)	14.12 (6.23)	12.69 (5.15)	13.76 (4.96)	17.14 (5.41)	14.65 (5.01)
BIS Attention	20.15 (2.76)	19.44 (2.71)	18.54 (2.22)	19.29 (3.60)	20.43 (2.23)	18.94 (3.44)
BIS Motor	24.46 (4.86)	26.25 (4.61)	24.54 (4.86)	26.59 (5.71)	26.71 (4.32)	23.18 (5.08)
BIS Non Planning	28.15 (7.02)	28.38 (5.81)	26.85 (5.64)	28.35 (6.76)	31.07 (3.99)	26.29 (4.65)
TRI CEP	20.92 (8.48)	21.31 (6.17)	20.23 (8.77)	23.12 (8.32)	30.43 (7.73)	23.00 (10.98)
TRI CBC	13.92 (6.65)	14.31 (6.50)	16.85 (8.96)	15.53 (8.01)	17.57 (8.12)	17.65 (8.07)

Alcohol consumption = average self-reported weekly alcohol consumption in UK units (1 UK unit = 10ml or 8g of pure alcohol); AUDIT = Alcohol Use Disorders Identification Test; BIS = Barratt Impulsivity Scales; TRI = Temptation and Restraint Inventory, CEP = Cognitive and Emotional Preoccupation, CBC = Cognitive Behavioural Control.

Table 3.S.2 Performance on the stop-signal task, shown separately for Control, Disinhibition, and Restraint groups, split by gender. Values are covariate adjusted means (standard error in brackets)

	Control		Disinhibition		Restraint	
	Male	Female	Male	Female	Male	Female
Reaction time to 'Go' cues (ms)	558 (33)	614 (29)	407 (33)	450 (27)	753 (34)	737 (27)
Number of errors on 'Go' trials	0.84 (0.47)	0.74 (0.54)	2.95 (0.47)	4.21 (0.52)	0.76 (0.49)	0.86 (0.52)
Number of Inhibition Errors	8.85 (2.06)	6.72 (2.09)	37.22 (2.08)	32.45 (2.03)	1.50 (2.14)	3.46 (2.03)

Table 3.S.3 Heart rate, blood pressure, self-reported mood and alcohol craving, shown separately for Control, Disinhibition, and Restraint groups, before and after completion of the stop-signal task, split by gender. Values are covariate adjusted means (standard error in brackets)

	Pre-Manipulation						Post-Manipulation					
	Control		Disinhibition		Restraint		Control		Disinhibition		Restraint	
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Heart Rate (bpm)	66.43 (3.15)	81.85 (3.48)	68.75 (3.19)	80.88 (3.37)	69.69 (3.28)	73.03 (3.36)	66.20 (2.58)	78.39 (3.25)	68.14 (2.61)	82.27 (3.14)	67.11 (2.69)	73.66 (3.14)
Systolic BP	128.23 (6.72)	115.58 (2.55)	111.05 (6.72)	112.20 (2.47)	120.52 (7.00)	110.42 (2.47)	117.00 (4.10)	100.20 (5.41)	120.38 (4.14)	102.16 (5.24)	115.08 (4.26)	105.65(5.24)
Diastolic BP	67.73 (2.84)	75.10 (2.91)	71.26 (2.87)	72.75 (2.81)	67.80 (2.95)	71.74 (2.81)	66.56 (3.51)	73.92 (3.21)	71.10 (3.56)	71.32 (3.11)	70.25 (3.66)	70.47 (3.11)
BMIS Pleasant	6.97 (1.63)	10.81 (1.19)	8.78 (1.69)	10.94 (1.07)	6.44 (1.68)	8.75 (1.08)	7.36 (1.81)	10.22 (1.65)	10.44 (1.87)	8.12 (1.50)	5.29 (1.86)	6.64 (1.50)
BMIS Arousal	14.23 (0.91)	13.42 (1.07)	15.34 (0.94)	14.97 (0.97)	15.64 (0.93)	14.92 (0.97)	13.79 (0.95)	13.00 (0.81)	14.86 (0.99)	13.67 (0.73)	14.60 (0.98)	14.39 (0.73)
BMIS Negative	4.74 (0.72)	2.93 (0.57)	4.50 (0.72)	3.79 (0.51)	5.53 (0.73)	4.50 (0.51)	4.30 (0.74)	2.93 (0.60)	3.89 (0.77)	4.03 (0.54)	5.46 (0.76)	5.09 (0.54)
BMIS Positive	7.53 (0.96)	8.28 (0.93)	8.16 (1.00)	9.18 (0.84)	7.95 (0.99)	8.41 (0.84)	7.85 (1.04)	7.56 (0.96)	9.04 (1.08)	7.30 (0.87)	6.89 (1.07)	7.12 (0.87)
AAAQ Obsessed	0.68 (0.30)	0.49 (0.30)	1.29 (0.31)	0.48 (0.24)	1.12 (0.32)	1.14 (0.24)	0.70 (0.26)	0.49 (0.25)	1.15 (0.26)	0.83 (0.21)	1.26 (0.27)	1.07 (0.12)
AAAQ Inclined	4.72 (0.53)	4.15 (0.43)	4.89 (0.54)	3.70 (0.41)	5.04 (0.56)	4.58 (0.41)	4.69 (0.53)	3.75 (0.45)	4.36 (0.53)	3.65 (0.44)	4.86 (0.55)	4.33 (0.44)
AAAQ Resolved	1.05 (0.33)	0.85 (0.28)	1.12 (0.34)	0.56 (0.27)	1.28 (0.34)	1.52 (0.27)	0.92 (0.34)	0.73 (0.26)	0.96 (0.34)	0.5(0.26)	1.23 (0.35)	1.17 (0.26)

Bmp = beats per minute; BP = blood pressure; BMIS = Brief Mood Introspection Scale; AAAQ = Approach and Avoidance of Alcohol Questionnaire.

Table 3.S.4 Participant responses to the stop-signal task. Values are covariate adjusted means (standard error in brackets)

	Control		Disinhibition		Restraint	
	Male	Female	Male	Female	Male	Female
Frustrating	3.21 (0.54)	3.57 (0.44)	2.55 (0.55)	3.47 (0.43)	2.93 (0.56)	3.35 (0.43)
Pleasant	1.91 (0.46)	1.96 (0.44)	1.47 (0.62)	1.52 (0.43)	2.29 (0.48)	2.52 (0.43)
Fighting an urge	2.44 (0.46)	2.09 (0.51)	1.38 (0.46)	2.40 (0.49)	3.02 (0.47)	2.10 (0.49)
Annoyed	2.46 (0.52)	1.61 (0.45)	1.81 (0.52)	2.21 (0.43)	2.32 (0.54)	2.39 (0.43)
Difficult	2.45 (0.42)	1.88 (0.36)	1.86 (0.43)	1.94 (0.35)	0.93 (0.44)	0.82 (0.35)
Irritating	2.54 (0.52)	2.78 (0.41)	2.56 (0.53)	3.22 (0.39)	2.84 (0.54)	3.11 (0.39)

Items were presented in a 7 point Likert scale, anchors were ‘not at all’ (1) and ‘extremely’ (7).

Table 3.S.5 Fluid consumed during the taste test and pleasantness ratings. Values are covariate adjusted means (standard error in brackets)

	Control		Disinhibition		Restraint	
	Male	Female	Male	Female	Male	Female
Beer cons (ml)	124.89 (23.88)	48.95 (11.88)	127.46 (24.16)	70.16 (11.50)	83.74 (24.86)	37.70 (11.49)
Juice cons (ml)	118.24 (23.84)	44.83 (13.96)	85.78 (24.12)	60.45 (13.52)	83.63 (24.82)	48.10 (13.51)
Beer pleasant	6.65 (0.74)	5.14 (0.75)	6.94 (0.75)	5.19 (0.73)	6.31 (0.79)	4.50 (0.73)
Juice pleasant	6.98 (0.55)	6.45 (0.59)	7.29 (0.55)	6.20 (0.57)	7.32 (0.57)	6.61 (0.57)

Chapter Four

P300 during response inhibition is associated with *ad-lib* alcohol consumption in social drinkers

This experiment was designed to examine the mechanisms behind the motivational bias manipulations (Jones et al. 2011a and Chapter Three). Using a within subjects design, participants were instructed to respond with restraint and also with normal response conflict (control group in Chapter Three). Event Related Potential measures were taken during the stop-signal task.

The results from this chapter have been submitted for publication to the Journal of Psychopharmacology. The source dipole analysis was submitted as supplementary materials, however in this case it is reported as part of the results. The format, but not the content, has been changed to be consistent with the rest of the thesis. At the time of thesis submission a decision on the manuscript has yet to be received.

The roles of the other three authors of the paper version in regards to publication are summarized below:

I designed the study, which was approved by Matt Field (primary supervisor).

Andrej Stancak provided training on EEG recording and Analysis. I collected the data with help from Paul Christiansen. I analysed the data and interpreted the results.

I wrote the manuscript. Matt Field, Paul Christiansen and Andrej Stancak gave helpful comments on the manuscript before submission.

4.1 Abstract

Rationale: Reduced amplitude of the cortical P300 event-related potential (ERP) component during response inhibition is associated with vulnerability to alcohol use disorders. However, there is little evidence to suggest that the P300 can fluctuate and whether these fluctuations are related to alcohol use

Method: In the current study, we investigated the effect of an experimental manipulation of response conflict on the amplitude of the P300 component during response inhibition, and examined whether individual differences in the amplitude of this P300 component would predict voluntary *ad-libitum* alcohol consumption, in social drinkers. Using a repeated measures design, sixteen participants performed a stop-signal task after receiving instructions that either emphasised or de-emphasised response conflict while EEG was concurrently recorded, before their *ad-libitum* drinking was assessed.

Results: Results revealed that task instructions had the predicted effects on behavioural indices of response inhibition and the associated P300 component. Most importantly, individual differences in the amplitude of P300 during response inhibition were negatively correlated with *ad-libitum* alcohol consumption. Source dipole analysis suggests the medial frontal cortex is the primary area that governs response inhibition. *Ad-libitum* alcohol consumption was also associated with activity in this brain region during inhibition, only under response conflict.

Conclusions: These findings provide the first experimental support for theoretical models that posit that reduced amplitude of the P300 during response inhibition is associated with alcohol-seeking behaviour in humans.

4.2 Introduction

Response inhibition - the ability to change or inhibit a motor response - enables organisms to adapt their behaviour in response to environmental demands. The ability to adapt behaviour in this way is a recognised component of executive functioning (Miyake et al. 2000) and ‘impulsivity’ (Bickel et al. 2012; Reynolds et al. 2006). Deficits in this ability are closely associated with various psychopathologies including alcohol use disorders (Goudriaan et al. 2006) and other substance use disorders (Verdejo-García et al. 2008). While there is some debate as to whether poor inhibitory control in alcohol use disorders is best characterised as a consequence of chronic heavy drinking or a pre-morbid risk-factor (de Wit 2009) a series of recent studies have demonstrated that poor inhibitory control may pre-date alcohol involvement and it serves as a risk factor for the development of alcohol use disorders later on in life (Nigg et al. 2006; Wong et al. 2006).

Response inhibition is typically assessed in the laboratory using computerised tasks such as the stop-signal task (Logan and Cowan 1984). In this task, participants make a rapid motor response in order to categorize visually presented ‘go’ stimuli, but on a minority of trials (typically 25%), they must inhibit their response whenever an auditory stop-signal is presented. The task thus establishes a response conflict between rapid responding and successful inhibition (Band et al. 2003). In two recent studies (Jones et al. 2011a; Jones et al. 2011b), we modified the task instructions before participants completed the stop-signal task in order to emphasize the importance of either rapid responding (at the expense of successful inhibition) or vice versa. This manipulation reduces the response conflict that is normally inherent in the task and instead places participants in either a disinhibited or restrained mental set, depending on whether instructions emphasized the importance of rapid responding or successful inhibition, respectively. In our previous studies, we demonstrated that experimentally-induced fluctuations in response inhibition influenced *ad-libitum* alcohol consumption in the laboratory in social drinkers. Furthermore, in both studies we found that individual differences in response inhibition were associated with alcohol-consumption, such that more disinhibited participants drank more alcohol. Therefore, these studies provide the first

experimental evidence that disinhibited ‘states’ have an immediate causal influence on alcohol consumption in human participants, as predicted by de Wit (2009).

Electrophysiological research into the brain mechanisms that underlie response inhibition has identified two important components of the event-related potential (ERP): the N200 and P300. The N200 is a negative peak which occurs in fronto-central regions between 200 ms and 300 ms after presentation of the stop-signal, whereas the P300 is a positive peak with a more posterior distribution which follows the N200 (Kok et al. 2004; Polich 2007; Polich and Criado 2006). The consensus is that when individuals have to actively inhibit a motor response both these components show an increased amplitude (Bokura et al. 2001; Dimoska et al. 2006) with successful inhibition associated with a P300 of greater magnitude than unsuccessful inhibition (Dimoska et al. 2006; Kok et al. 2004).

The degree of response conflict within the stop-signal task influences the amplitude of N200 and P300 ERPs during response inhibition (Ramautar et al. 2004). However, whilst N200 is often elicited during response inhibition tasks such as the stop-signal, this component is sometimes larger during unsuccessful compared to successful inhibition (Kok et al. 2004). Therefore, the functional specificity of this component is still unclear (Dimoska et al. 2006). On the other hand, the amplitude of P300 is consistently larger during successful compared to unsuccessful inhibition (Dimoska et al. 2003; Kok et al. 2004; Ramautar et al. 2004). In relation to alcohol use disorders, reduced amplitude of the P300 (but not N200) during response inhibition is thought to represent a component of the alcoholic phenotype (Cohen et al. 1997; Euser et al. 2011; Kamarajan et al. 2005a). Consistent with this, blunted P300 during response inhibition is present in individuals considered ‘at risk’ for the development of alcoholism such as children of alcoholics (Kamarajan et al. 2005b). Furthermore, the P300 during response inhibition is attenuated in alcoholics who are prone to relapse compared to alcoholics who are able to maintain abstinence (Glenn et al. 1993). Therefore, this evidence suggests that a blunted P300 during response inhibition may index the underlying processes that cause excessive alcohol consumption, in particular poor inhibitory control.

Importantly, no previous study has examined whether electrophysiological markers of response inhibition are associated with subsequent *ad-lib* alcohol consumption in

social drinkers. Our primary aim in the present study was to investigate this relationship. Our secondary aim was to corroborate previous demonstrations that an experimental reduction of response conflict during the stop-signal task would reduce the amplitude of the P300 during response inhibition (Ramautar et al. 2004) by using our previous methodology (Jones et al. 2011a; Jones et al. 2011b) in which we manipulated task instructions in order to (de)emphasise the conflict between rapid responding and successful inhibition, and thereby influence behavioural indices of response inhibition.

To achieve these aims, participants performed a stop-signal task on two separate occasions: once with an emphasis placed on cautious responding and successful inhibition, and once with standard instructions that emphasised the conflict between rapid responding and successful inhibition. Immediately after completing the stop-signal task, participants completed a bogus ‘taste test’ in which their *ad-libitum* alcohol consumption was assessed. Our primary hypothesis was that individual differences in the amplitude of the P300, and a behavioural index of response inhibition (Stop-signal Reaction Time; Logan et al. 1997), would both be correlated with alcohol consumption, albeit only when participants completed the stop-signal task following standard instructions which emphasised the conflict between rapid responding and successful inhibition. Our secondary hypothesis was that the amplitude of P300 during successful inhibition would be significantly attenuated following instructions which placed the emphasis on successful restraint (and thereby reduced response conflict) compared to standard instructions which emphasised response conflict (cf. Ramautar et al. 2004).

4.3 Methods

Subjects

Sixteen participants (7 females, 9 males, mean age 20.50 ± 2.56 years) took part in the study. Inclusion criteria were: social drinking (consumption of alcohol at least once per week), no history of any neurological / neuropsychiatric disorders, a liking for beer and fruit juice, and aged between 18 and 30. Participants were asked to

refrain from consuming caffeine for two hours, and from alcohol for the entire day, before attending the laboratory. Participants were recruited via advertisements placed around the University campus and on the intranet. All participants provided informed consent before taking part in the study, which was approved by the University of Liverpool Research Ethics Committee and carried out in accordance with the Declaration of Helsinki

Procedure

Experimental sessions took place in EEG laboratories in the School of Psychology, University of Liverpool, between the hours of 12 and 6pm. Task instructions (conflict or restraint, see below) and drink type (see below) were counterbalanced across sessions. In the first session participants provided informed consent before completing a questionnaire battery consisting of: two week alcohol Timeline Follow-Back diary (Sobell and Sobell 1992), the Alcohol Use Disorders Identification Test (Saunders et al. 1993), the Temptation and Restraint Inventory (Collins and Lapp 1992), and the Barratt Impulsiveness Scales (Patton et al. 1995).

The electrode cap was fitted before participants were seated inside a sound attenuated chamber, approximately 1.5 meters from the stimulus presentation monitor. The stop-signal task (Logan and Cowan 1984) was programmed using Inquisit 3.0 (Millisecond Software: Seattle, WA), and presented on a standard PC with a 15 inch monitor. The task began with a fixation point '+' that was presented for 500 ms. Following this, one of two 'Go' stimuli were presented, either an 'X' or 'O'. Participants were required to press one key upon presentation of 'X' and a different key upon presentation of 'O', using different fingers of the right hand. The Go stimuli were uninterrupted on 75% of trials, and a stimulus timeout of 1000 ms was used (incorrect responses, or those that occurred after the timeout period were coded as errors of omission). On 25% of trials an auditory 'Stop' signal was presented at one of two delays (150 ms or 250 ms) after onset of the Go stimulus, which signalled that participants should inhibit their motor response. Failures to inhibit were coded as errors of commission. There was an inter-trial interval of 1500 ms. The task was split into 6 blocks of 64 trials, with 48 Go trials and 16 Stop trials (8 at 150 ms and 8 at 250 ms) in each block. The task took around 45 minutes to complete.

Participants were given different instructions for the stop-signal task in different experimental sessions, based on those used in our previous studies (Jones et al. 2011a; Jones et al. 2011b). In the ‘conflict’ condition, participants were instructed to ‘respond as quickly as possible to the Go stimuli, and if you hear the tone you should inhibit your response. The tone is infrequent and you may not always be able to inhibit. You should not wait for the tone’. Note that these are ‘standard’ instructions for the stop-signal task because they set up a conflict between rapid responding and successful inhibition (Logan and Cowan 1984). In the ‘restraint’ condition participants were instructed: ‘respond as carefully and accurately to the stimuli as possible. The stop tone is infrequent and random and you should be careful to inhibit your response to this tone’. Therefore, participants were instructed to inhibit their responses when stop-signals were presented in both sessions, but the ‘restraint’ instructions place more emphasis on successful inhibition; in previous studies, these instructions led to slower reaction times to go cues and a higher rate of successful inhibitions (Jones et al. 2011a; Jones et al. 2011b).

Following the stop-signal task, the EEG cap and electrodes were removed before participants completed the Approach and Avoidance of Alcohol Questionnaire (AAAQ) and the Brief Mood Introspection Scale (BMIS) (Mayer and Gaschke 1988). Data from these questionnaires are not reported here but we note that, as in our previous studies (Jones et al. 2011a; Jones et al. 2011b), there were no significant differences between conflict and restraint conditions on either questionnaire. Participants then completed a bogus taste test, which was identical to that used in our previous studies. They were given 250 ml of chilled beer (either ‘Kronenbourg 1664’ or ‘Becks’, both ABV 5%) and 250 ml of fruit juice (either J20 apple and blueberry or J20 blackcurrant and raspberry), in unmarked glasses. They were instructed to consume as much or as little as they liked of each drink in order to rate them on 10 adjectives (such as bitterness, fruitiness etc). Taste ratings were not analysed as their only purpose was to obscure the true purpose of the taste test, which was to measure voluntary alcohol consumption. The dependent variable was the volume of beer consumed as a percentage of total fluid.

Participants returned for the second session four to seven days later and they again completed the stop-signal task while EEG activity was recorded. This time, task instructions were different from those used in the first session (so those who had

received ‘conflict’ instructions in the first session received ‘restraint’ instructions in the second session, and vice versa). Participants then completed the AAAQ and BMIS followed by the bogus taste test, but with different drinks to those used in the first session. At the end of the study, participants received £20 or course credit, before being debriefed and discharged.

EEG recording

EEG activity was recorded continuously using 64 scalp electrodes based on the extended 10/20 system using a Biosemi ActiveTwo system (Biosemi, Amsterdam, Netherlands). The electrode cap was aligned using four anatomical landmarks; nasion, occipital protuberance and left and right pre-auricular points. Electrode gel was used to ensure that electrode to skin impedance was always below 10 k Ω . Vertical electrooculograms (EOG) were recorded in parallel with EEG signals above and below the right eye using flat disc electrodes, and all signals were recorded continuously with 1024 Hz sampling frequency. The recording bandpass filter was set at 0.1 – 200 Hz similar to prior studies (Enoch et al. 2001). Reference electrodes were placed on the right mastoid.

Data reduction and analysis

Stop-signal Reaction Time (SSRT) was computed using the integration method (Logan et al. 1997), such that higher values of SSRT are indicative of poor inhibitory control.

Brain Electrical Source Analysis (BESA) v. 5.2 program (MEGIS, Germany) was used to analyse EEG data. EOG artefacts were removed by principal component analysis procedure (Berg and Scherg 1994), and muscle artefact rejection was completed manually by visual inspection before averaging. Data were spatially transformed to reference-free data using the common average reference method. Continuous EEG data was broken down into epochs of 1100 ms (100 ms pre-stimulus presentation and 1000 ms post-stimulus) with ERPs time-locked to the onset of the go stimulus during stop-signal trials, on which participants successfully inhibited motor responses to the stop-signal. Epochs containing artefacts were removed from analysis, as were data from trials in which commission errors were made. The remaining epochs were averaged across all six blocks of the task.

Filtering was done on the averaged data at 0.5 – 40 Hz. For individual electrode analysis, grand averages were exported to Matlab R2009a (Mathworks: Natick, MA).

In accordance with methods used in previous studies (e.g. Kamarajan et al., 2005a) the P300 component was identified as the largest positive peak following presentation of the stop-signal (this corresponded to the period 350 - 400 ms on trials with a 150 ms stop-signal delay, and the period 550-600 ms on trials with a 250 ms stop-signal delay). The N200 component was identified by searching backwards for the first negative peak occurring prior to the P300 (Nieuwenhuis et al., 2003) , which corresponded to the period 240-280 ms on trials with a 150 ms stop-signal delay, and the period 380-420 ms on trials with a 250 ms stop-signal delay. The amplitude of the N200 and P300 was calculated as the mean amplitude within the specific epochs described above. We computed mean amplitude instead of peak amplitude, because the former is preferable when there are unequal numbers of trials in different experimental conditions, which was the case in the present study because we only computed ERPs during stop-signal trials on which participants were successful at inhibiting their responses (Luck, 2005). For both P300 and N200, we averaged ERPs across 150 ms and 250 ms stop-signal delays for individual electrodes along the mid-line (Fz, Cz and Pz). Midline electrodes were chosen in accordance with previous research examining inhibition P300 in alcoholics and other drug users (Gamma et al. 2005; Kamarajan et al. 2005a).

4.4 Results

Demographics, craving and mood.

The mean age of the sample was 20.50 (\pm 2.56). Participants consumed on average 25.35 (\pm 19.5) units of alcohol per week (1 unit = 8g alcohol) and had a mean AUDIT score of 12.75 (\pm 4.14). There were no significant differences in craving or mood in the different experimental conditions (these data are not shown but are available on request).

Stop-signal task (see Table 4.1)

To examine the effects of experimental condition on response inhibition, paired-samples t-tests were conducted on mean Go reaction times and Stop-signal Reaction Time (Table 4.1). Task instructions affected Go reaction times ($t(15) = 7.70, p < .01$) and SSRT ($t(15) = -3.40, p < .01$). Compared to ‘conflict’ instructions, ‘restraint’ instructions produced slower reaction times to Go cues and a greater SSRT, which is consistent with our previous studies in which task instructions were manipulated in this way (Jones et al., 2011a, b).

P300 ERP component at midline electrodes (see Figure 4.1)

Figs. 4.1 A and B show isopotential maps of N200 and P300 components in grand average ERPs in conflict (Fig. 4.1A) and restraint (Fig. 4.1B) conditions for both stop-signal delays (150 ms and 250 ms). The N200 component showed a negative spatial maximum at fronto-central electrodes with some left-side predominance. The P300 component showed the strongest positive maximum at centro-parietal electrodes. To investigate effects of task instructions on ERP components, electrodes Fz, Pz and Cz were analysed in detail. The grand average ERPs for these electrodes are shown in Fig. 4.1C for 150 ms (left column) and 250 ms (right column) latencies.

To explore the effects of task instructions on the P300 component, amplitudes of P300 potentials were averaged across the two stop-signal delays. A 3 (electrode: Fz, Cz, Pz) \times 2 (condition: conflict, restraint) \times 2 (condition order: conflict first, restraint first) mixed design ANOVA was performed. There were significant main effects of both electrode ($F(2,14) = 23.06, p < .01$) and condition ($F(1,14) = 4.97, p < .05$). The electrode \times condition interaction was not statistically significant ($F(2,14) = 0.30, p > .10$), and neither was the electrode \times condition \times order interaction ($F(2,28) = 0.68, p > .10$).

To explore the main effect of condition, we performed planned comparisons using paired samples t-tests on P300 amplitudes in the different experimental conditions. The P300 amplitude was significantly larger following conflict instructions compared to restraint instructions at all electrode sites (Fz, $t(15) = 1.82, p < .05$; Cz, $t(15) = 1.79, p < .05$; Pz, $t(15) = 1.78, p < .05$), as hypothesised.

Effects of stop-signal task instructions and delays on the amplitude of the N200 component revealed no significant effect of condition, or condition x electrode interaction ($ps > 0.10$).

Electrophysiological and behavioural associations with alcohol-seeking (Figure 4.2)

Following conflict instructions, the association between P300 amplitude (averaged across the three electrode sites, over the two delays) during successful inhibition and *ad-libitum* alcohol consumption was statistically significant ($r = -.71, p < .01$).

However, this association was not significant following restraint instructions ($r = .05, p > .1$). Consistent with this, the association between Stop-signal Reaction Time and *ad-libitum* alcohol consumption was significant following conflict instructions ($r = .43, p < .05$) but not following restraint instructions ($r = .17, p > .10$). These correlations suggest that increased *ad-lib* alcohol consumption is associated with both reduced amplitude of P300 during response inhibition, and with a behavioural index of response inhibition. Finally, SSRT and P300 amplitude during successful inhibition were significantly correlated following conflict instructions ($r = -.67, p < .01$) but not following restraint instructions ($r = -.26, p > .1$).

4.5 Discussion

P300 amplitude during successful response inhibition was reduced when task instructions placed the emphasis on successful inhibition before participants completed a stop-signal task. More importantly, when participants performed the task after receiving standard instructions (which emphasised the conflict between rapid responding and successful inhibition), reduced amplitude of the P300 during successful response inhibition was associated with increased voluntary *ad-libitum* alcohol consumption. To our knowledge, this is the first study to experimentally manipulate electrophysiological markers of response inhibition by using modified task instructions, and it is the first demonstration that P300 amplitude during response inhibition is associated with subsequent alcohol consumption measured in the laboratory.

We demonstrated that when participants completed the stop-signal task after instructions which emphasised the importance of successful inhibition, and therefore reduced the usual conflict in the task (between rapid responding and successful inhibition), the amplitude of P300 during successful inhibition was significantly reduced. This finding is consistent with a previous report (Ramautar et al. 2004), in which a different method was used to reduce conflict within the task by increasing the frequency of stop-signal trials from 25% of trials to 75%. Furthermore it is consistent with a hypothesis by Kok et al., (2004) who suggested that P300 may represent an ‘urgent inhibitory brake’. By contrast, our differential task instructions did not influence the amplitude of the N200 during response inhibition.

Our most important finding was the demonstration that individual differences in the amplitude of the P300 during successful response inhibition were negatively correlated with participants’ *ad-lib* alcohol consumption, which was assessed immediately after participants completed the stop-signal task. However, this was only the case when participants completed the task after receiving standard instructions (which emphasised the response conflict between rapid responding and successful inhibition), but not when task instructions emphasised successful inhibition at the expense of rapid responding. This suggests that the P300 during response inhibition is directly associated with momentary fluctuations in the motivation to drink alcohol, such that individuals in whom the P300 during response inhibition is of relatively small amplitude are more likely to drink alcohol to excess at that moment in time. These results complement previous studies which demonstrate that reduced amplitude of the P300 during response inhibition is a biomarker for alcohol problems (Cohen et al. 1997; Euser et al. 2011; Kamarajan et al. 2005a; Kamarajan et al. 2005b), and is a risk-factor the development of alcohol use disorders later in life (Justus et al. 2001; Kamarajan et al. 2005b). Our results extend this finding by demonstrating that individual differences in the amplitude of the P300 during response inhibition are associated with the volume of alcohol that participants choose to consume at that exact moment in time, and therefore they support theoretical models (de Wit 2009) and recent findings (Jones et al. 2011a; Jones et al. 2011b) which demonstrate that inhibitory control can fluctuate within individuals, and that both behavioural and electrophysiological markers of inhibitory control are associated with laboratory measures of the motivation to drink alcohol.

The observed negative correlation between the amplitude of the P300 during successful inhibition and the behavioural measure of inhibitory control (stop-signal reaction time) is also important as it validates P300 as a biomarker of inhibitory control, albeit only when participants complete the stop-signal task after receiving standard instructions for the task which emphasise the equal importance of rapid responding to go signals and successful inhibition to stop-signals, thereby establishing a response conflict. It is perhaps unsurprising that the amplitude of P300, stop-signal reaction time and *ad-libitum* alcohol consumption were not inter-correlated following the modified 'restraint' instructions, as these instructions deliberately remove the response conflict from the task and place the emphasis on successful inhibition, with rapid responding only of secondary importance. Therefore, the present results are informative as they reveal that response conflict during the stop-signal task has a major influence on behavioural and electrophysiological indices of response inhibition, although these instructions also render the task invalid as a measure of inhibitory control.

Limitations of our study include the use of a simplified version of the original stop-signal task (Logan and Cowan 1984). We opted to use only two stop-signal delays (150 and 250 ms) in order to generate reliable patterns of electrophysiological activity at each stop-signal delay. One disadvantage of this approach is that we were unable to map activity across a broader range of inhibitory performance, as the original stop-signal task employs a range of delays which make inhibition very easy (e.g. 50 ms) in addition to delays which make inhibition almost impossible (e.g. 450 ms). Future studies of this type should use a broader range of stop-signal delays in order to investigate if task instructions influence the magnitude of the P300 during successful response inhibition at a range of stop-signal delays. In addition, as this was a pilot study we recruited a relatively small number of participants, and therefore the magnitude of the effects reported here may differ if larger samples are studied in future replications of our work. However, we note that similar studies have investigated both group differences, and individual differences in ERP components associated with inhibitory control with comparable sample sizes (Gamma et al. 2005; Petit et al. 2012; Stancak et al. 2012).

To summarise, this study is the first to examine the association between the magnitude of the P300 during response inhibition, and subsequent ad-lib alcohol

consumption. Results suggest that an experimental manipulation of response conflict can affect the magnitude of the P300 during successful inhibition, which is consistent with previous reports. Most importantly, the amplitude of the P300 during successful inhibition was negatively correlated with subsequent alcohol consumption, such that individuals in whom the P300 amplitude was relatively small tended to drink more alcohol when given *ad-libitum* access to it. These results extend previous studies of the P300 in the context of response inhibition in alcoholics and individuals ‘at risk’ for alcoholism.

4.6 Supplementary analysis: Source analysis of inhibition

Whilst ERP data has good temporal resolution, using single electrodes does not allow for good spatial analysis. Any given scalp potential at a select electrode would represent a summation of potentials from different cortical regions with unknown weight. Therefore, ERPs were analysed using multiple source dipole analysis (Scherg and von Cramon 1986). Multiple source dipole analysis entails building a model encompassing several equivalent source dipoles placed into different cortical regions.

In the present study, equivalent source dipoles were fitted using sequential strategy (Hochstetter et al. 2001; Stancak et al. 2002), which involves fitting source dipoles based on latency peaks in the global field power starting with the component showing the shortest latency. In source localisation, the ellipsoid head model was used, and the conductivities were set as follows: skin = 0.33 S/m, skull = 0.0042 S/m, cerebrospinal fluid = 1.0 S/m, and brain parenchyma = 0.33 S/m. The accuracy of source dipole modelling in localising cortical sources using spherical head models is approximately 1.0 cm (Cuffin et al. 2001).

The source models were built using grand averages across conditions separately for 150 ms and 250 ms stop-signal delays. Seven distinct sources were identified (Fig 4.S.1). Each source model (150 ms and 250 ms) accounted for approximately 92% of variance in activity during successful inhibitions

Auditory and Visual sources

Two sources were located bilaterally in the visual cortex and accounted for the initial P100 and N160–180 components of the visual evoked potentials, the occurrence of these coincides with initial presentation of the ‘go’ stimulus. Two sources were located bilaterally in the auditory cortex, most likely the superior temporal gyri, accounting for the auditory evoked potential associated with presentation of the stop-signal.

Sources related to action and inhibition

Activation in three distinct sources occurred during response inhibition. There was a source located around left sensorimotor cortex region, and accounted for negativity in the left precentral region and positivity in posterior parietal electrodes peaking at 278.2 ± 13.7 ms. This source likely accounted for increasing motor preparedness in contralateral sensorimotor cortex prior to the processing of the auditory stop-signal.

A further source was located in the medial-frontal cortex (MFC). This equivalent source dipole accounted for the strong negative potential maximum which co-occurred with maxima of auditory components located in bilateral superior temporal gyri. The negative maximum at vertex was followed by a positive component occurring at 382.2 ± 33.1 ms at the 150 ms stop-signal delay and at 494.7 ± 24.5 ms at the 250 ms stop-signal delay. This positive component of the MFC dipole accounted for part of the positive P300 component peaking at 378.5 ± 9.8 ms at electrode Cz in the 150 ms latency. However, the positive maxima over the vertex were not fully accounted for by the MFC source. In particular, the late potential component (>500 ms in the 250 ms condition) was accompanied by positivity at the vertex and negativity in the lower occipital region and neck, which were best modelled by a final source most likely the cerebellum. These two sources accounted for a large portion of the P300 component regularly seen during successful inhibition (Kok et al. 2004).

Differences between experimental conditions

The source representing medial frontal cortex activity showed greater activation during inhibition in the conflict condition ($t(15) = -2.40, p < .05$), using 2000 permutation methods (Maris and Oostenveld 2007), shown by the grey area in

Fig.4.S.1B. Finally activity in the MFC was associated with *ad-libitum* alcohol consumption in the conflict group ($r = -.57, p < .05$) (Fig.4.S.1C), mirroring the findings with scalp data presented.

Table 4.1 Dependent measures from the stop-signal task, shown separately across conditions. Values are means \pm SD.

	Conflict	Restraint
Go reaction time (ms)	458.38 \pm 53.05	650.17 \pm 108.59
SSRT	168.19 \pm 21.97	206.44 \pm 30.87

Figure 4.1 Grand average isopotential maps and a comparison of ERPs along the midline electrodes for both conflict and restraint conditions.

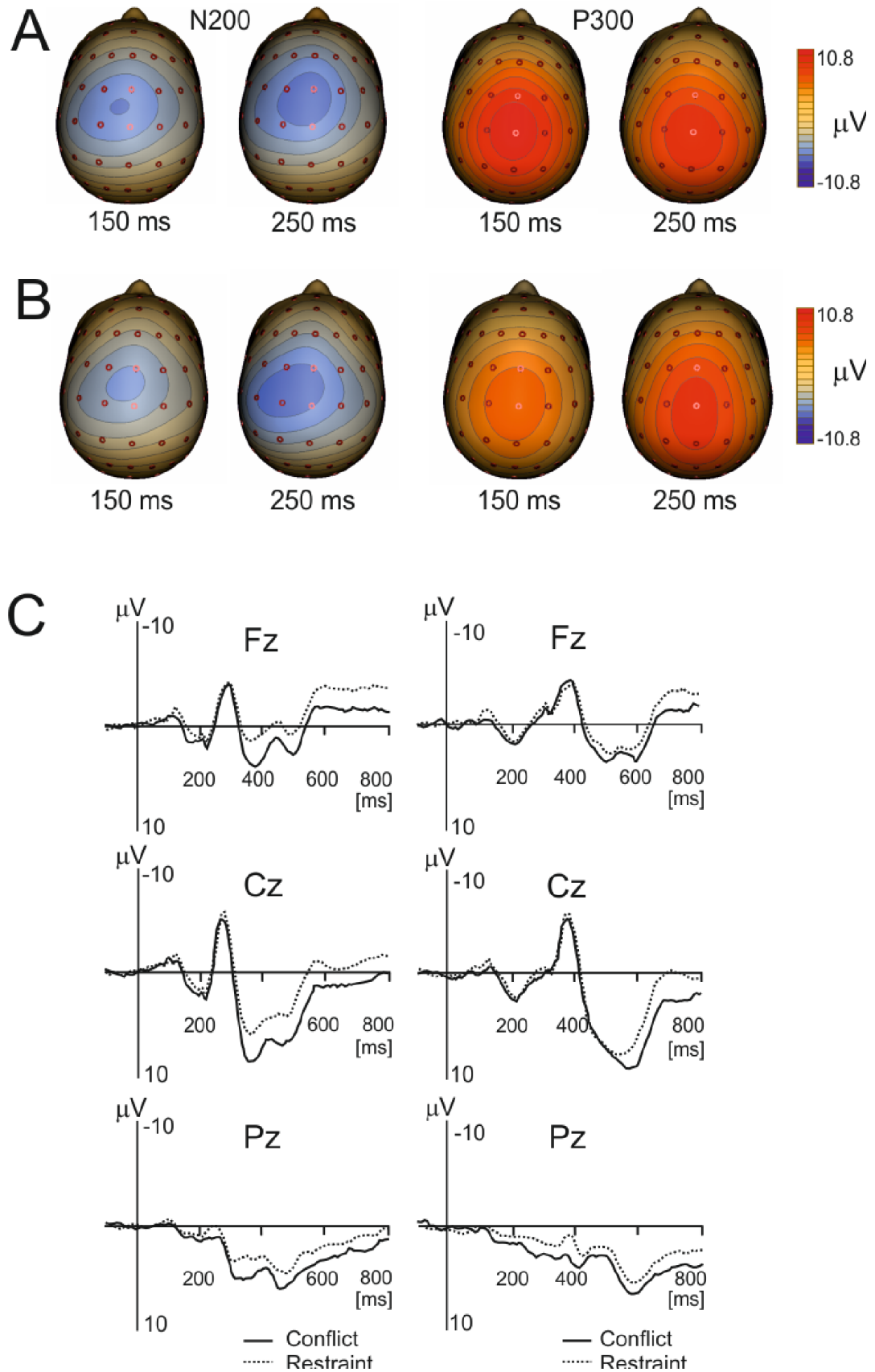


Figure 4.2. The intracorrelations between P300 amplitude, SSRT and beer consumption for both conflict and restraint conditions.

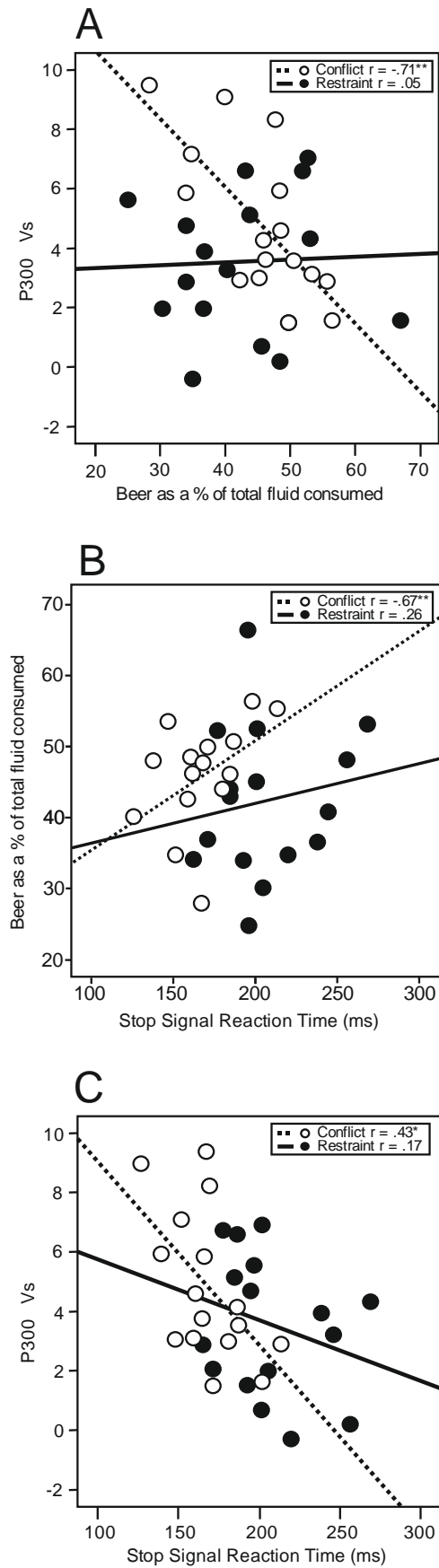
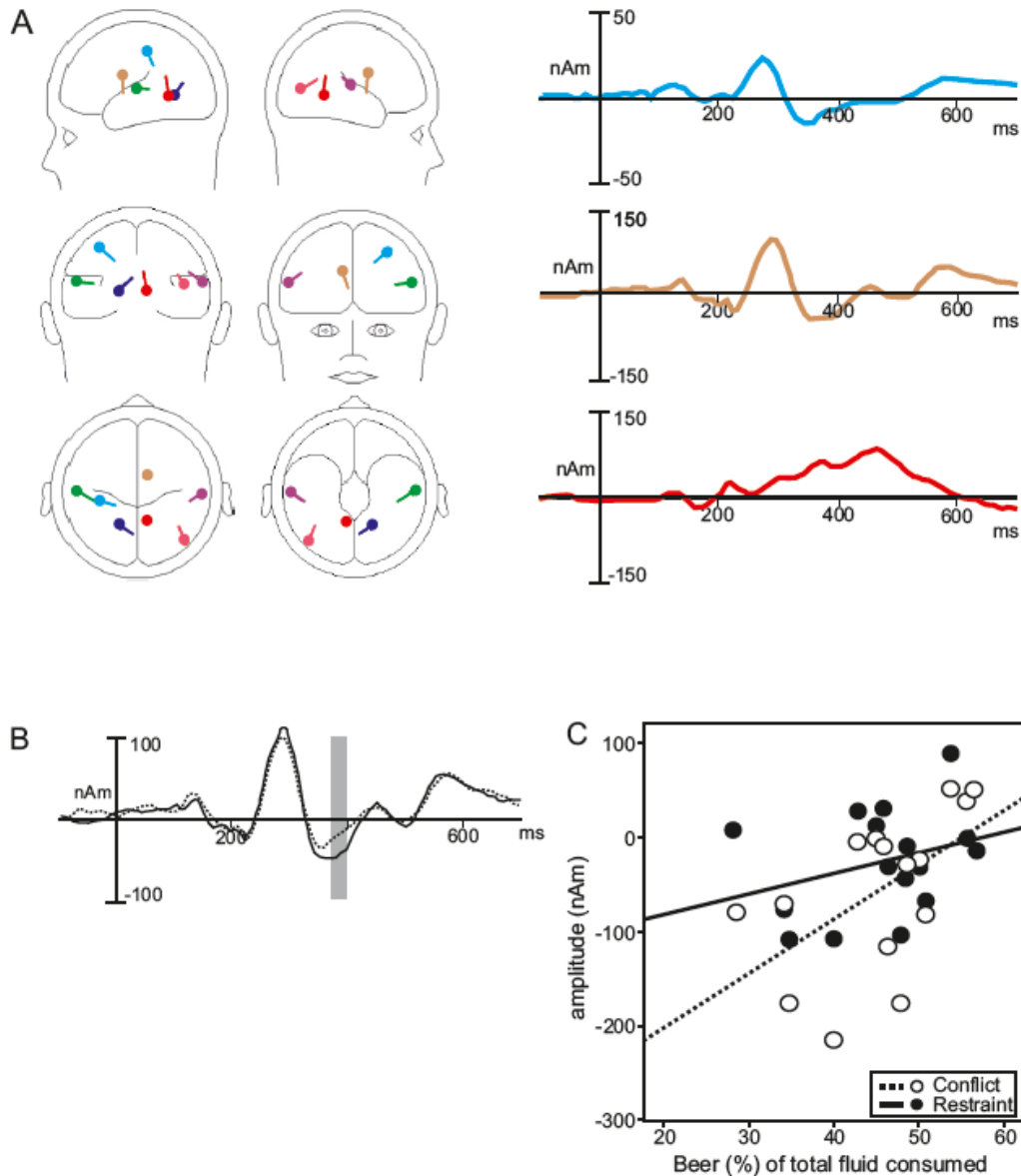


Figure legends.

Fig 4.1A. Grand average isopotential maps of N200 and P300 components in the conflict instruction at stop-signal task delays of 150 ms and 250 ms. The topographic maps show distribution of electrical potentials as seen from top view. Negativity is plotted in blue colour. **B.** Isopotential maps of N200 component and P300 components in the restraint instruction for both stop-signal task delays. **C.** A comparison of ERPs along the midline electrodes (Fz, Cz and Pz) shown for both task instructions for 150ms (left panel) and 250ms (right panel) stop-signal delays. Conflict and restraint instruction potentials are plotted using bold and dotted lines, respectively.

Fig 4.2A. The correlation between the P300 amplitude during inhibition and *ad-libitum* alcohol consumption. **B.** The correlation between the SSRT and *ad-libitum* alcohol consumption. **C.** The correlation between the P300 amplitude during inhibition and Stop-signal reaction time. (* $p < .05$, ** $p < .01$)

Figure 4.S.1 Supplementary Analysis: Source Dipole Analysis



S.1.A Source analysis showing in glass brain projections locations of seven distinct source dipoles during stop trials at 150 ms delay. Grand average source waveforms representing the three sources involved during inhibition, averaged across task instructions. **S.1.B** A comparison of source dipole waveform for MFC across condition (full line: conflict; dashed line: restraint) in 150 ms Stop signal trials, grey-shaded rectangles represent significant differences in levels of activation at corrected $p < 0.05$. **S.1.C** The correlation between the strength of anterior cingulate cortex activity in 150 ms Stop signal trials and ad-libitum alcohol consumption (Negative values correspond to spatial positivity).

Chapter Five

The effects of cue-specific inhibition training on alcohol consumption in heavy social drinkers

These experiments were designed to examine whether inhibition could be trained specifically to alcohol cues. In response to a critique of the Jones et al., (2011a) study, Houben et al., (2011a) argued that the motivational bias strategy would unlikely result in long term changes in alcohol-seeking. In Experiment One I examined whether any fluctuations in disinhibition could influence alcohol-seeking outside of the laboratory, using a one week follow up. Experiment Two examined the causal relationship between oculomotor inhibition and alcohol-seeking in the laboratory.

This chapter has been accepted for publication in the Journal of Experimental and Clinical Psychopharmacology, and is in press at the time of thesis submission. The reviews requested a supplementary materials section be created; this is presented as such in the thesis. The format, but not the content, has been changed to be consistent with the rest of the thesis.

The roles of the authors of the paper version in regards to publication are summarized below:

I designed both studies, which were approved by Matt Field (primary supervisor). I collected and analysed the data. I wrote the manuscript. Matt Field gave comments on the manuscript before submission and following initial peer review.

5.1 Abstract

Training social drinkers to exercise motor inhibitory control leads to a reduction in alcohol consumption. However, it is unclear if participants should attempt to exercise inhibitory control in the presence of alcohol-related cues, or if non-specific inhibition training is equally effective. It is also unclear if comparable effects can be demonstrated by training oculomotor inhibitory control. We trained motor inhibition in the context of a modified stop-signal task (Experiment One) and oculomotor inhibition in the context of a modified anti-saccade task (Experiment Two), before investigating the influence of these manipulations on alcohol consumption. Results from Experiment One demonstrated that training motor inhibition in the presence of alcohol-related cues led to reduced *ad-libitum* alcohol consumption in the laboratory, but not self-reported drinking in the week after training. These effects were seen in contrast to a control group that received no inhibition training and a further control group that were trained to inhibit only in the presence of neutral cues; alcohol consumption did not differ between the latter two groups. In Experiment Two, training of oculomotor inhibition in the presence of alcohol-related cues led to slowed eye movements towards target cues on catch trials, but it did not influence the proportion of inhibitory failures, and had no influence on alcohol consumption in the laboratory. We conclude that training participants to exercise inhibitory control in the presence of alcohol-related cues can reduce alcohol consumption, but effects are transient and are only seen when motor, but not oculomotor inhibition is trained.

5.2 Introduction

Inhibitory control – the ability to stop, delay or change a behaviour - is one of the most well researched components of impulsivity and executive functioning (Bickel, Jarmolowicz, Mueller, Gatchalian, and McClure, 2012). This construct can be measured in the laboratory using computer tasks such as the stop-signal task (Logan and Cowan, 1984), Go/No-go task (Fillmore and Rush, 2002) and the anti-saccade task (Hallett, 1978). While all three tasks are thought to measure inhibitory control, they appear to measure slightly different aspects of it (Schachar et al., 2007; Verbruggen and Logan, 2008). Theoretical models posit that deficits in inhibitory control are associated with substance use disorders, including alcohol abuse and dependence (Dawe and Loxton, 2004; de Wit, 2009; Goldstein and Volkow, 2002). This is supported by cross sectional research showing that performance on the stop-signal task and Go/No-go tasks can differentiate between alcoholics and controls, and between heavy and light social drinkers (Christiansen, Cole, Goudie, and Field, 2012; Goudriaan, Oosterlaan, de Beurs, and van den Brink, 2006; Verdejo-García, Lawrence, and Clark, 2008). Furthermore in some populations, such as individuals with Attention Deficit Hyperactivity Disorder (ADHD), oculomotor inhibitory control (as measured by the anti-saccade task) is associated with individual differences in alcohol consumption (Weafer, Milich, and Fillmore, 2011).

Recently, research has focussed on the notion that inhibitory control can fluctuate within individuals, much like any other state, and that ‘abrupt environmental, physiological or emotional events ... may cause transient ‘state’ changes in either self-control or inhibition that may result in re-initiation of drug use’ (de Wit, 2009). In support of this, we demonstrated that experimentally-induced fluctuations in inhibitory control can have an immediate impact on alcohol-seeking in social drinkers (Jones et al., 2011a, b). In these studies, we demonstrated that participants who had been primed with a restrained mental set drank significantly less beer in the laboratory, compared to participants who had been primed with a disinhibited mental set.

If inhibitory control plays a causal role in the development and maintenance of alcohol use disorders, it is possible that training heavy drinkers to improve their

inhibitory control might serve as a useful adjunct to established interventions to reduce drinking. However, given that heavy drinking is often triggered by alcohol-related environmental cues (e.g. the sight and smell of beer), and that such cues lead to transient impairments in inhibitory control (Gauggel et al., 2010), it is important to establish if participants can be trained to exercise inhibitory control when faced with such cues. This was recently investigated in a series of studies by Houben et al (2011a, 2012). In these studies, participants performed a Go/No-go task in which alcohol-related and neutral cues were presented. One group of participants were consistently required to inhibit motor responses when alcohol cues were presented, but to respond rapidly to neutral cues; these contingencies were reversed in a different group of participants. In both studies, Houben et al. (2011a, 2012) demonstrated that, compared to participants who had to exercise inhibition in response to neutral cues, participants who exercised inhibition when faced with alcohol cues reported drinking significantly less alcohol in the week immediately following the task. Furthermore, in the first study (Houben et al., 2011a) there was a non-significant trend for participants in the alcohol cue inhibition group to drink significantly less beer in the laboratory compared to participants in the neutral cue inhibition group.

To summarise, previous findings suggest that (1) non-specific but transient increases in inhibitory control may reduce alcohol-seeking in the laboratory (Jones et al., 2011a, b) ; (2) participants must be trained to exercise inhibition specifically in response to alcohol cues, in order for inhibition training to reduce alcohol consumption outside of the laboratory (Houben et al., 2011a; 2012). It is of theoretical and practical importance to examine whether cue-specific inhibition training can lead to cue-specific improvements in inhibitory control, and if these improvements lead to reduced alcohol consumption. In the present studies we examined the effects of training inhibitory control in response to alcohol cues on *ad-libitum* alcohol consumption in the laboratory. Our aim was to integrate Houben et al's (2011a; 2012) research with our own (Jones et al., 2011a, b) to examine whether specific training of inhibitory control to alcohol cues would a) cause measurable improvements in inhibitory control in response to alcohol cues, and b) lead to reductions in alcohol-seeking. We used modified stop-signal and anti-saccade tasks

(Eagle, Bari, and Robbins, 2008; Roberts, Fillmore, and Milich, 2011) so that we could track changes in inhibitory control, specific to cues, over time.

5.3 Experiment One

Houben et al. (2011a, 2012) provided the first experimental evidence that training inhibitory control in the presence of alcohol cues could prompt a reduction in alcohol consumption. However, two issues complicate interpretation of these results. Firstly, participants were trained to either inhibit responding when alcohol cues were presented, and respond rapidly to neutral cues ('beer/ no-go group'), or vice versa (beer/ go group). The observed group differences in alcohol consumption might be attributed to training of inhibitory control in response to alcohol cues in the 'beer/ no – go' group, but they might also be attributed to rapid, disinhibited responding to alcohol cues in the 'beer/ go group'. In order to distinguish between these alternative explanations, we included a third group of participants who received equivalent exposure to alcohol and neutral cues, but who were never required to inhibit their responding ('disinhibition' group; cf. Houben et al., 2011b). The second important issue is that Houben et al. (2011a; 2012) used a Go/No-go task to train inhibitory control in the presence of alcohol-related cues. Whilst they did not make direct comparisons between groups on their training task, they measured changes in inhibitory control in the presence of alcohol cues using a modified stop-signal task (administered after training) and they did not detect between-group differences on this task. However, these two tasks measure distinct components of response inhibition (action restraint versus action cancellation, respectively; see Schachar et al., 2007), so it is possible that training of action restraint does not influence action cancellation (and potentially, vice versa).

In this experiment, we used a modified stop-signal task to train inhibitory control in the presence of alcohol cues, and to track improvements in inhibitory control over the course of training. Participants had to rapidly categorise alcohol-related and neutral pictorial cues and were randomly allocated to one of three experimental groups. In the 'alcohol restraint' and 'neutral restraint' groups, participants were

instructed to inhibit their motor response whenever they heard an auditory tone. These stop-signal tones were paired with alcohol-related pictures on 90% of trials in the ‘alcohol restraint’ group, but were paired with neutral pictures on 90% of trials in the ‘neutral restraint’ group. In the ‘disinhibited’ group, tones appeared equally often after the alcohol-related and neutral pictures, but participants in this group were instructed to ignore the tone, and therefore participants in this group were never required to inhibit their responses. We hypothesised speeded reaction times to neutral cues and slowed reaction times to alcohol cues in the ‘alcohol restraint’ group compared to the ‘neutral restraint’ group, whereas the disinhibited group should become faster overall (regardless of cue type). We also predicted that, as training progressed, the ‘alcohol restraint’ group would make more inhibition errors on the neutral stop trials than the alcohol stop trials, with the reverse pattern expected in the ‘neutral restraint’ group. Most importantly, we predicted that alcohol consumption – both *ad-libitum* consumption of beer in the laboratory, and self-reported alcohol consumption in the week following the study – would be lowest in the alcohol restraint group, intermediate in the neutral restraint group, and highest in the disinhibited group because the latter group were trained to respond rapidly to alcohol cues, but unlike the neutral restraint group they were never required to inhibit their responding.

5.4 Method

Participants

Participants were recruited from the staff and student population at the University of Liverpool, with advertisements placed around campus and on the University Intranet. Ninety participants (49 Female), with a mean age of 20.79 (\pm 2.65) were recruited. Inclusion criteria included: heavy social drinking (defined as drinking of excess of UK government guidelines, 14 units per week for women, 21 units for men; 1 unit = 8 grams of pure alcohol (Edwards, 1996)), a liking for beer, no history of self-reported alcohol abuse or alcohol problems, and being aged between the ages of 18 and 30. Participants were informed that they were signing up for an experiment on

‘reaction times and taste perception’. Experimental group allocation was randomized in both experiments. All participants provided informed consent before taking part in the studies, which were approved by the University of Liverpool Research Ethics Committee.

Materials and measures

Questionnaires

Participants were given a questionnaire battery consisting of two week Timeline Follow-Back diary (Sobell and Sobell, 1992) in order to assess their alcohol consumption over the two weeks prior to the experiment, this was followed by the Alcohol Use Disorders Identification Test (Saunders, Aasland, Babor, Fuente, and Grant, 1993), Temptation and Restraint Inventory (Collins and Lapp, 1992), and the Barratt Impulsivity Scale version 11 (Patton, Stanford, and Barratt, 1995). The ‘right now’ version of the Approach and Avoidance of Alcohol questionnaire (McEvoy, Stritzke, French, Lang, and Ketterman, 2004) was administered to assess craving on three distinct subscales; Inclined / Indulgent, Obsessed / Compelled and Resolved / Regulated. Finally the Brief Mood Introspection Scale (Mayer and Gaschke, 1988) was administered to assess mood and arousal on four continuums: pleasant-unpleasant, arousal-calm, positive-tired, and negative-relaxed.

Following the stop-signal task participants completed a post-task questionnaire taken from Jones et al, (2011b). This comprised six statements concerning participants’ impressions of the task (e.g. frustration, irritation), and participants responded using an 8-point Likert scale with the anchors ‘not at all (0)’ and ‘extremely (7)’.

Stop-signal task with cues.

The task was programmed using Inquisit 3.0 (Millisecond software, 2008). Each trial began with a fixation cross (‘+’) presented in the centre of the screen for 500ms. Following this fixation cross either an alcohol-related or neutral picture appeared in the centre of the screen. Participants were required to quickly categorise the content of the picture by pressing a key labelled ‘X’ for an alcohol related picture, or a key labelled ‘O’ for a neutral picture. These trials were ‘go’ trials.

On 50% of trials an auditory tone occurred at one of four latencies (50ms, 150ms, 250ms and 350ms) after the picture appeared. For the ‘alcohol restraint’ and ‘neutral

restraint' groups, these were stop-signals that signified that participants should inhibit their motor response on that trial, and wait for the next trial. If participants responded within a 2000 ms timeout period this was classed as an inhibition error. For the 'disinhibition' group, participants were instructed to ignore the tone and to categorise all pictures.

The task was split into four blocks; a baseline block of 48 trials and three experimental blocks of 80 trials. The baseline block comprised an equal number (12) of four types of trials: alcohol go (no tone), neutral go (no tone), alcohol + tone and neutral + tone. The main purpose of this block was to familiarise participants with the task, however we note there were no significant differences between the Alcohol and Neutral restraint groups in inhibition errors or reaction times. The experimental blocks were different for experimental groups and were structured as follows. For the 'alcohol restraint' group, each block comprised four alcohol 'go' trials, 36 alcohol 'stop' trials (9 at each stop latency), 36 neutral 'go' trials and 4 neutral stop trials (one at each stop latency). For the 'neutral restraint' group these weightings were reversed. For the disinhibition group the tone occurred on half the alcohol and half the neutral picture trials, yet participants were told to ignore the tone whenever it occurred. The task utilized the same picture set used in previous laboratory research (Field and Eastwood, 2005; Jones et al., 2012), which included 10 alcohol and 10 neutral pictures, all 100mm high x 145 mm wide .

Taste test

Participants were given 250ml of chilled beer (Budweiser Budvar, 5% ABV) and fruit juice drink (J20 orange and passion fruit) and told explicitly they could 'drink as much or as little as they liked' in order to rate the drinks on 10 adjectives (e.g. pleasantness, fruitiness, bitterness). Beer as a percentage of total fluid consumed was calculated and used as the primary measure of alcohol-seeking in accordance with our previous studies (Jones et al., 2011a, b).

Procedure.

Participants completed the initial questionnaire battery (including AAAQ and BMIS) before completing the stop-signal task. Participants then completed the AAAQ and BMIS again and the post-task questionnaire before the bogus taste test in which *ad-libitum* alcohol consumption was measured. Participants then completed a funnelled

debriefing, which included an assessment of their awareness of the purpose of the stop-signal task (see supplementary materials for description of method, and results). Participants were then being given a one-week alcohol consumption diary and instructed to return it exactly one week later. At the end of the study, participants were debriefed and received £10 or course credit for taking part.

5.5 Results

Descriptive statistics (Supplementary Table 5.S.1).

Across the entire sample, the average AUDIT score was 14.65 (SD = 5.14), and self-reported weekly alcohol consumption was 30.56 (SD = 14.77) units in Males, and 22.90 (SD = 9.33) units in Females. Univariate ANOVAs were conducted to investigate group differences on demographic variables and the questionnaires administered at the beginning of the study. There were no significant differences between groups on any of these variables ($ps > .15$)

Craving, Mood and post-test feedback (Supplementary Table 5.S.2A)

Group differences in scores on the AAAQ were investigated using a mixed design ANOVA with within subjects factors of AAAQ subscale (3 : Inclined, Obsessed, Resolved) and time (2 : baseline, post stop-signal task), and a between subjects factor of group (3: alcohol restraint, neutral restraint, disinhibition). There was a main effect of subscale ($F(2,172) = 291.53, p < .01$). There was also a significant group X time interaction ($F(2,172) = 4.01, p < .05$) and a significant subscale X time interaction ($F(2,172) = 3.56, p < .05$). Performing the analysis separately for each group revealed a significant main effect of time ($F(1,29) = 6.77, p < .05$) in the alcohol restraint group only. Overall, scores on all three subscales were reduced in the alcohol restraint group following the stop-signal task compared to before the task.

There were no significant interactions involving group or time on the BMIS, and there were no between-group differences on any of the items in the post-task questionnaire ($ps > .1$).

Cued stop-signal task performance (Table 5.1.A).

Reaction times on 'Go' trials. Individual trials with errors or extreme outliers (trials with RTs \pm 3SDs of the mean) were removed from analysis (0.69 % of total trials). Reaction times to alcohol and neutral cues on 'go' trials were contrasted in the three groups in the first and last training blocks of the stop-signal task (blocks one and three) using a three way mixed design ANOVA with within-subject factors of time (2 : block 1 / block 3) and cue type (2: alcohol / neutral) and a between subjects factor of group (3: alcohol restraint, neutral restraint, disinhibition). The hypothesised time X cue X group interaction was statistically significant ($F(3,87) = 15.83, p < .01$). The effect was explored with ANOVAs conducted separately for each group. Within the alcohol restraint group, the time X cue interaction was statistically significant ($F(1,29) = 26.02, p < .01$). Paired samples t-tests revealed a significant slowing of reaction times to alcohol cues from block one to block three ($t(29) = -3.84, p < .05$), and a significant speeding of reaction times to neutral cues from block one to block three ($t(29) = 2.25, p < .05$). However, there was no significant time X cue interaction in either the neutral restraint or disinhibited groups ($F_s < 2.37, p_s > .1$). Between group contrasts revealed that the disinhibited group had the fastest reaction times in the final block, for both types of cues ($p_s < .01$). In the final block, reaction times to alcohol cues were slower in the alcohol restraint group compared to the neutral restraint group ($t(29) = 5.87, p < .01$), whereas this group difference was reversed for neutral cues ($t(29) = -6.50, p < .01$).

Inhibition errors. Alcohol restraint and neutral restraint groups differed on the number of alcohol cue and neutral cue stop trials, so we first calculated the number of stop-signal trials on which participants failed to inhibit their response and expressed this as a percentage of the total number of stop-signal trials for each cue type within each block. These analyses did not include participants in the disinhibition group as this group were never required to inhibit their responding. The percentage of inhibition errors was analysed using a mixed design 2 x 2 x 2 ANOVA, with within-subject factors of time (2: block 1, block 3) and cue (2: alcohol, neutral) and a between subjects factor of group (2: alcohol restraint, neutral restraint). As predicted, the time X cue X group interaction ($F(1,58) = 10.38, p < .01$) was statistically significant. Post-hoc ANOVAs performed separately on each group

yielded significant time X cue interactions in both groups (alcohol restraint, $F(1,29)=5.47, p <.05$; neutral restraint, $F(1,29)=4.93, p <.05$).

Within the alcohol restraint group, inhibition errors to alcohol cues reduced from the first to the third block ($t(29)=1.91, p <.05$), whereas inhibition errors to neutral cues increased from the first to the third block ($t(29)=-2.16, p <.05$). In the neutral restraint group inhibition errors to alcohol cues increased from the first to the third block ($t(29)=-2.08, p <.05$) whereas there was no change in inhibition errors to neutral cues from the first to the third block ($t(29)=0.89, p >.10$). Furthermore, between group comparisons revealed that the alcohol restraint group made fewer inhibition errors to alcohol cues in both blocks ($ts > 2.23, ps <.01$) whereas the neutral restraint group made fewer inhibition errors to neutral cues in both blocks ($ts > 2.28, ps <.01$).

Overall, these data confirm that the experimental manipulation was successful.

Compared to both alcohol restraint and neutral restraint groups, participants in the disinhibited group responded to both types of cues more quickly. The alcohol restraint group became progressively slower to respond to alcohol cues and faster to respond to neutral cues, with the opposite pattern seen in the neutral restraint group. Finally, the alcohol restraint group made fewer inhibition errors in response to alcohol cues than the neutral restraint group.

Alcohol consumption in the laboratory (Fig 5.1).

Group differences in beer consumption as a percentage of total fluid were analysed using univariate ANOVA, with a between-subjects factor of group (3: alcohol restraint, neutral restraint, disinhibited). The main effect of group was statistically significant ($F(2,87)=6.40, p <.01$). Bonferroni post-hoc comparisons confirmed that the alcohol restraint group drank significantly less beer than the neutral restraint group ($p <.01$) and the disinhibited group ($p <.05$). There was no significant difference between the neutral restraint group and the disinhibited group ($p >.10$). There was no significant group effect on overall beverage consumption ($F(2,87)=2.22, p >.10$). Additional analyses revealed that gender did not influence this pattern of results. Overall these results demonstrate that, following the experimental manipulation, the alcohol restraint group consumed significantly less beer than the neutral restraint and disinhibited groups, who did not differ from each other. These

group differences were specific to beer consumption, and did not reflect a generalised group difference in overall beverage consumption.

Self-reported alcohol consumption at one week follow-up.

Seventy eight participants (86.6%) (Alcohol restraint = 28, Neutral restraint = 26, Disinhibition = 24) returned the alcohol consumption diary one week after the experimental session. Group differences in total alcohol consumption (calculated as the number of units consumed) were analysed with a univariate ANCOVA, with experimental group (3: alcohol restraint, neutral restraint, disinhibition) as a between-subjects factor, and weekly alcohol consumption before the experiment (obtained from the timeline followback diary administered at baseline) entered as a covariate. The main effect of group was not statistically significant ($F(2,74) = 0.19$, $p > .10$) (Alcohol restraint = 29.86 ± 18.29 units, Neutral restraint = 25.65 ± 11.13 , Disinhibition 26.73 ± 24.34). Additional analyses indicated that gender did not influence these results.

5.6 Experiment Two

The anti-saccade task measures an aspect of response inhibition that is distinct from that measured by the stop-signal and Go/No-go tasks (Logan and Irwin 2000). Saccadic eye movements directed towards stimuli which abruptly appear in peripheral vision are innate whereas motor categorisation responses are not, which arguably makes the anti-saccade task particularly sensitive for assaying inhibitory control deficits in certain populations such as those with ADHD (Roberts, et al., 2011), in whom poor oculomotor inhibition is associated with increased alcohol consumption (Weafer, et al., 2011). Furthermore, performance on the task is known to be influenced by acute alcohol (Roche and King, 2010), pharmacotherapy for ADHD (O'Driscoll et al., 2005) and task instructions (Taylor and Hutton, 2009), which suggests that this measure of inhibitory control is malleable. Importantly, in contrast to several studies on motor response inhibition (Houben et al., 2011a, 2012; Experiment One in this manuscript), no previous studies have investigated the

influence of cue-specific oculomotor inhibition deficits on alcohol consumption in the laboratory.

In the second experiment we modified the basic anti-saccade task by varying the predictive relationship between picture type (alcohol-related vs. neutral) and the type of ocular movement (pro-saccade or anti-saccade) required on that trial, in order to train participants to associate oculomotor inhibition with either alcohol-related or neutral cues. The task has previously been modified to measure fluctuations in oculomotor inhibition in response to motivational and emotional cues (Hardin et al., 2009). As this was the first experimental study to modify the task in order to train inhibitory control in response to alcohol-related cues, we opted for a more simple experimental design compared to that used in experiment one. In the ‘alcohol restraint’ group, participants made an anti-saccade on 80% of trials in which an alcohol-related picture was presented, but a pro-saccade on 80% of trials in which a neutral picture was presented. These contingencies were reversed in the ‘neutral restraint’ group. Our primary hypothesis was that participants in the ‘alcohol restraint’ group would have slower pro-saccade reaction times and make fewer inhibition errors (anti-saccade errors) on alcohol cue trials compared to the ‘neutral restraint’ group, whereas this group difference would be reversed for neutral cue trials. Our secondary hypothesis was that the ‘alcohol restraint’ group would consume less beer than the ‘neutral restraint’ group during the bogus taste test administered in the laboratory. As this was an initial proof of principle study exploring the utility of inhibition training using a modified anti-saccade task, we did not include a disinhibition group or follow-up assessment of alcohol consumption after participants left the laboratory, as we had done in the first experiment.

5.7 Method

Participants

Participants were recruited using the same methods and inclusion criteria as experiment one. Individuals who wore glasses were excluded due to the use of eye-

tracking equipment. Sixty participants (32 Female), with a mean age of 21.18 (\pm 3.03) were recruited.

Materials and Equipment

Questionnaires

Participants completed the same questionnaire battery at both baseline and post-test as in experiment one.

Cued saccade task.

The task was programmed using Inquisit 3.0 (Millisecond software, 2008) and presented on a 19 inch monitor. Participants' eye movements were measured using an ASL Eye-Trac D6 (Applied Science Laboratories, Bedford, USA) at a sampling rate of 120Hz. Each trial began with the presentation of a picture in the centre of a black screen for 2000ms, this picture was either alcohol-related or neutral in content. For the final 200ms of picture presentation a green or red cross was superimposed over the picture. The colour of this cross informed the participant to perform either a pro (green) or anti (red) saccade to a small white target cross. After 2000ms the picture and coloured cross disappeared and the white target cross appeared 30mm from either the left or right outer edges of the screen. As in previous research participants were required to fixate on this cross on pro-saccade trials, or to fixate on the mirror opposite location on anti-saccade trials (Hallett, 1978). Correct responses were defined as a saccade followed by a stable fixation (eye movements which were stable within one degree of visual angle for at least 100ms; see Mogg et al., 2003) to the appropriate region of the screen, defined as a 15mm x 15mm region surrounding the target cross location on pro-saccade trials or the mirror image location on anti-saccade trials. Anti-saccade errors were defined as a saccade ending in a fixation to the target cross (Roberts, et al., 2011). Similar to experiment one, we measured changes in inhibitory performance using the dependent measures proportion of inhibition errors (anti-saccade errors) and also latencies to fixate on the target position, because slower latencies for gaze to arrive at the position (target cross or mirror opposite position) can be assumed to reflect a delay in initiating the saccade, or initiating a saccade in the wrong direction before correcting it. Trials timed out at 2000ms, and any fixations which occurred after the timeout period were classified as errors.

The task began with a block of 40 practice trials to familiarise participants with the task, in which picture type (alcohol or neutral), saccade type (pro or anti) and target position (left or right) were fully counterbalanced. There were no significant group differences on inhibition errors or reaction times in this block. Following this three blocks of 80 trials were presented. Each block contained an equal number of alcohol-related and neutral pictures, and pro- and anti-saccade trials, however the contingency between picture type and saccade type varied in the different experimental groups. In the ‘alcohol restraint’ group, anti-saccade trials occurred on 32 of 40 alcohol pictures and 8 of 40 neutral pictures, whereas pro-saccade trials occurred on 8 of 40 alcohol pictures and 32 of 40 neutral pictures. In the ‘neutral restraint’ group, these contingencies were reversed. The same picture sets were used as in experiment one.

Procedure.

Participants completed the initial questionnaire battery before completing the cued-saccade task. Participants then completed the AAAQ and BMIS again along with post-task feedback before the bogus taste test in which *ad-libitum* alcohol consumption was measured. Finally they completed a funnelled debriefing (see Supplementary materials for results) and received £10 or course credit for taking part.

5.8 Results

Group characteristics (Supplementary Table 5.S.3)

Across the entire sample, the average AUDIT score was 13.83 (SD = 4.81), and self-reported weekly alcohol consumption was 38.26 (SD = 25.28) units in Males, and 24.02 (SD = 40.07) units in Females. Independent samples t-tests were conducted to investigate group differences in demographic variables and the questionnaires administered at the beginning of the study. There were no significant differences between groups on any of these variables ($ps > .13$)

Craving, Mood and post-test feedback (Supplementary Table 5.S.2B).

There were no significant main effects of group, or group x time interactions, on any of the AAAQ or BMIS subscales. Similarly, there were no significant group differences on the post-task questionnaire.

Cued anti-saccade task performance (Table 5.1.B).

Fixation latency. Trials were excluded if fixations to the target position occurred faster than 50 ms after target onset, as these were considered anticipatory (Wexler, 2005). We also excluded fixation latencies that were extreme outliers (± 3 SDs from the participants' mean). Following exclusion of these trials, we removed all data from two participants (one in each group) as they had an outlying high rate of missing data ($>32\%$). In the remainder of the sample 13.29% of trials were excluded as anticipation/time-out, errors or outliers. Fixation latencies were analysed separately for each trial type (anti-saccade, pro-saccade) using 2 x 2 x 2 mixed design ANOVAs with within subjects factors of time (2: block one, block three) and cue type (2: alcohol, neutral), and a between subjects factor of group (2: alcohol restraint, neutral restraint). For the pro-saccade trials there was a significant time X cue X group interaction ($F(1,56) = 10.21, p < .01$). Performing a 2 (time) x 2 (cue type) ANOVA separately for each group revealed a time X cue interaction for the alcohol restraint group ($F(1,28) = 12.43, p < .01$) but not the neutral restraint group ($F(1,28) = 2.65, p > .10$). Paired samples t-tests demonstrated that the alcohol restraint group became slower making pro-saccades following alcohol cues over time ($t(29) = -2.12, p < .05$). There were no significant changes in the neutral restraint group. For anti-saccade trials the time X cue X group interaction was not statistically significant ($F(1,58) = 0.58, p > .1$).

Anti-saccade errors. As with experiment one, percentage of inhibition errors for each cue were used and analysed using a mixed design 2 x 2 x 2 ANOVA, with within-subject factors of time (2: block 1, block 3) and cue (2: alcohol, neutral) and a between subjects factor of group (2: alcohol restraint, neutral restraint). The hypothesised time X cue X group interaction was not significant ($F(1,56) = 0.21, p > .10$).

These data suggest that the experimental manipulation was partially successful in altering oculomotor inhibitory control. The manipulation led to slowing of pro-saccades predicted by alcohol cues in the alcohol restraint group. However there were no significant cue effects on anti-saccade errors in either group.

Alcohol consumption in the laboratory.

Group differences in beer consumption as a percentage of total fluid were analysed using an independent samples t-test, which revealed no significant group difference (Alcohol restraint $41.63\% \pm 15.52$, Neutral restraint $46.11\% \pm 9.57$; $t(58) = 0.50$, $p > .10$). Total amount of fluid consumed did not differ between experimental groups either (Alcohol restraint = 208.17 ± 144.23 , Neutral restraint = 194.40 ± 107.36 ; $t(58) = 0.68$, $p > .10$). Additional analyses did not reveal any gender differences. Overall, these results demonstrate that the cue-specific training using a modified anti-saccade task did not affect *ad-libitum* alcohol consumption in the laboratory.

5.9 Discussion

The aim of these studies was to extend previous experimental research by examining whether training motor and oculomotor inhibition in the presence of alcohol cues would lead to reductions in alcohol consumption. While the effects of the cue-specific training were successful at improving motor inhibitory control and reducing alcohol consumption in experiment one, the effects of oculomotor inhibition training were much weaker and did not influence alcohol consumption in experiment two. Comparison of the results from the two experiments in the context of the previous literature has a number of important theoretical implications which in turn have implications for the refinement of inhibitory control training as an intervention to reduce heavy drinking.

The primary finding from experiment one is that training inhibitory control in the presence of alcohol cues in heavy drinkers led to improvements in inhibitory control and a reduction in *ad-libitum* alcohol consumption in the laboratory. This is the first study to show a significant reduction in *ad-libitum* alcohol consumption following cue-specific inhibition training (but see Houben et al., 2011a, who reported a non-significant trend in the same direction). These results complement previous findings that manipulations of inhibitory control in a non-specific manner can also reduce alcohol-seeking in the laboratory (Jones et al., 2011a, b). Taken together these findings support models of addiction which posit that poor inhibitory control is

associated with heavy drinking (Dawe and Loxton, 2004; de Wit, 2009; Goldstein and Volkow, 2002). Furthermore, they support arguments made by de Wit (2009), that response inhibition can fluctuate within individuals and that these fluctuations can *cause* the (re)initiation of alcohol consumption in sober individuals.

These results build upon previous findings from Houben and colleagues (2011a, 2012) who demonstrated reductions in drinking at one week follow-up among heavy drinkers who had been trained to inhibit their responding in the presence of alcohol cues using a modified Go/No-go task. While we did not replicate these effects on self-reported drinking behaviour at one-week follow-up, we speculate that this may be attributable to the different tasks used to modify inhibitory control. As discussed, the stop-signal and Go/No-go tasks capture subtly different sub-components of inhibitory control. Compared to the Go/No-go task, demands on inhibitory control are greater in the stop-signal task because this task requires participants to cancel a response which has already been initiated (Eagle, et al., 2008; Verbruggen and Logan, 2008), which may explain why our manipulation affected alcohol consumption immediately, in the laboratory, but these effects did not persist at follow-up. In contrast to our findings, Houben et al. (2011a, 2012) found reduced alcohol consumption at one-week follow-up, but only a trend towards significance on *ad-libitum* drinking in the laboratory, following training with a modified Go/No-go task. Importantly, Houben et al. (2012) found that the effects of modified Go/No-go training were mediated by changes in automatic alcohol associations, representing a devaluation of alcohol stimuli, rather than improvements in inhibitory control *per se*.

In order to translate these findings into a viable treatment intervention, it is important to examine whether multiple sessions of inhibition training can lead to long-lasting reductions in alcohol consumption outside of the laboratory, because single sessions of cognitive training are unlikely to produce long-lasting benefit (contrast findings reported by Field et al., 2007 and Schoenmakers et al., 2010, in the context of attentional bias modification). As noted above, it may be that a combination of both the stop-signal and Go/No-go tasks, modified to improve inhibitory control in the presence of alcohol cues, may have the greatest impact as these may conjointly increase cue-specific inhibitory control and alter automatic affective associations, thereby devaluing alcohol (Veling, Holland, and van Knippenberg, 2008).

In contrast to the positive results shown in experiment one, in experiment two we failed to observe any impact of oculomotor inhibition training on alcohol consumption in the laboratory. Oculomotor inhibition training made participants slower to direct their attention to target cues on pro-saccade ‘catch’ trials, but it did lead to improvements in oculomotor inhibitory control in the presence of alcohol-related cues. Therefore, our failure to detect effects of this manipulation on alcohol consumption is unsurprising given that the manipulation did not lead to clear improvements in cue-specific inhibitory control. There are at least two explanations for these results. Firstly, it may be that deficits in oculomotor response inhibition are only causally related to alcohol consumption in subgroups of participants, such as those with ADHD (Weafer, et al., 2011). Alternatively, even if the relationship between (poor) oculomotor response inhibition and heavy drinking proves to be robust and generalizable across populations, the relationship may not be a causal one in which case training of oculomotor inhibitory control would be futile. Self-administration of alcohol involves motor responses (e.g., picking up a glass) rather than oculomotor responses, so from this perspective it makes sense to focus training on motor inhibition.

One limitation of both experiments reported here is that we recruited heavy drinking students, rather than older adults from the wider community. We recruited students in accordance with Houben et al.’s (2011a; 2012) as well as our own (Jones et al., 2011a, b) previous studies. Heavy drinking young adults, including students, have been shown to have deficient inhibitory control (Christiansen et al., 2012) and they are at high risk of developing alcohol related problems in the future (Bonomo, Bowes, Coffey, Carlin, and Patton, 2004; Jennison, 2004). Therefore, they are suitable populations for basic research investigating causal influences on alcohol consumption. However, college students are generally not motivated to reduce their alcohol consumption, which is possibly why our inhibitory control training did not lead to reductions in drinking outside of the laboratory. Future extensions of this work should recruit different populations such as older adults who are motivated to limit their drinking, or alcohol-dependent individuals, in order to evaluate inhibitory control training as a potential treatment intervention.

In summary, the present results demonstrate that training motor inhibition in the presence of alcohol cues caused improvements in inhibitory control, and led to

reduced *ad-libitum* alcohol consumption in the laboratory. However, when individuals were trained to exercise oculomotor inhibition in the presence of alcohol cues, this did not influence alcohol consumption. Neither intervention led to a reduction in alcohol consumption over a one-week follow-up period. Future research should attempt to clarify whether these interventions can be modified in order to reduce drinking over longer periods of time among individuals who are motivated to reduce their alcohol consumption.

5.10 Supplementary analysis:

Awareness of experimental contingencies.

Method

During the funnelled debriefing, participants were instructed to select from eight possible options in order to complete the sentence ‘The computer task was designed to.....’. Response options included ‘train me to inhibit to alcohol cues’ (correct response for participants in the ‘alcohol restraint’ groups), ‘train me to inhibit to neutral cues’ (correct response for participants in the ‘neutral restraint’ groups), and ‘measure reaction times to the target stimuli’ (correct response for participants in the ‘disinhibition’ group in experiment one). There were five other response options which were not correct for any of the participants (e.g. ‘train me to think more quickly’).

Results

Experiment One

Twenty five participants (27.7%) were aware of the purpose of the task (12 from the Alcohol restraint group, eight from the Neutral restraint group and five from the Disinhibition group, $\chi^2(2, 90) = 4.10, p = .12$). When we removed data from these participants and repeated the analyses, the group difference in *ad-libitum* alcohol consumption in the laboratory was still significant ($F(2,62) = 5.34, p < .01$) with

Bonferroni post hoc analysis showing significant differences between Alcohol Restraint and Neutral Restraint groups ($p < .05$) and Alcohol Restraint and Disinhibited ($p < .05$) groups. There was no significant difference between Neutral Restraint and Disinhibited groups ($p > .10$). The group difference in self-reported alcohol consumption at one-week follow-up was still non-significant ($F(2,53) = 0.61$, $p > .10$).

Experiment Two

Five participants (8.3%) were aware of the purpose of the task (two from the Alcohol restraint group and three from the Neutral restraint group, $\chi^2(1, N = 60) = 0.22$, $p = .64$). When we removed data from these participants and repeated the analyses, the group difference in ad-libitum alcohol consumption in the laboratory was still non-significant ($t(53) = -1.13$, $p > .10$).

Figure 5.1: Beer as a percentage of total fluid consumed for experimental groups following the cued stop-signal task, in experiment one. Values are means (standard errors).

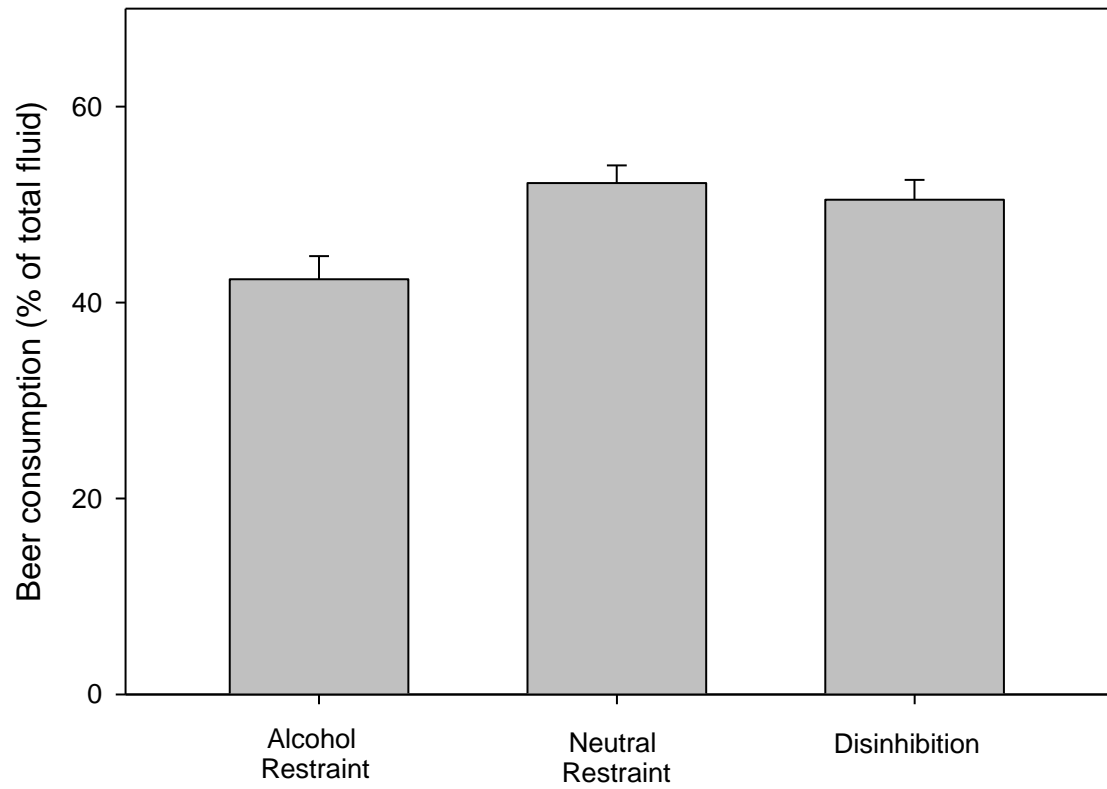


Table 5.1. Reaction times and proportion of inhibition errors over time, shown separately for groups, across experiment one and two. Values are means (standard deviations).

	Block one			Block three		
A. Experiment one	Alcohol	Neutral	Disinhibition	Alcohol	Neutral	Disinhibition
Alcohol Go RT	735.61 (155.02)	681.22 (160.93)	407.72 (71.53)	858.34 (172.69)	605.32 (125.12)	406.32 (57.90)
Neutral Go RT	630.06 (121.76)	829.07 (212.91)	424.05 (70.09)	597.89 (87.54)	805.69 (172.77)	416.21 (54.05)
Alcohol Stop (%)	2.87 (4.09)	10.83 (18.20)		1.58 (2.15)	20.00 (24.03)	
Neutral Stop (%)	10.83 (18.20)	2.96 (5.00)		19.17 (22.44)	2.32 (4.07)	
B. Experiment two	Alcohol	Neutral		Alcohol	Neutral	
Alcohol pro-saccade RT	279.21 (53.35)	276.89 (69.89)		312.81 (73.88)	280.96 (106.04)	
Neutral pro-saccade RT	295.85 (63.19)	263.24 (52.42)		276.38 (79.35)	308.09 (188.86)	
Alcohol anti-saccade RT	366.35 (104.05)	349.62 (91.87)		355.09 (102.83)	355.77 (89.14)	
Neutral anti-saccade RT	349.09 (76.07)	343.84 (64.19)		366.80 (100.12)	364.34 (91.96)	
Alcohol anti-saccade (%)	11.32 (8.97)	12.07 (13.56)		12.61 (9.39)	16.81 (17.76)	
Neutral anti-saccade (%)	12.50 (12.94)	11.64 (8.64)		12.50 (12.50)	13.78 (12.78)	

A. Go RT = reaction time on go trials. Stop (%) = proportion of inhibition errors.

B. pro-saccade RT = reaction time to fixate on target stimuli on pro-saccade trials. anti-saccade RT = reaction time to fixate on mirror opposite position of target stimuli on anti-saccade trials. anti-saccade (%) = proportion of inhibition errors on anti-saccade trials.

Supplementary Materials.

Supplementary Table 5.S.1: Participant characteristics in experiment one. Values are Means (standard deviations).

	Alcohol restraint (N=30)	Neutral restraint (N=30)	Disinhibition (N=30)	F value (2,89)	p- Value
Gender (M : F)	13 : 17	14 : 16	14 : 16	-	-
Age	20.47 (2.49)	21.27 (3.05)	20.63 (2.40)	0.75	.43
Alcohol cons.	26.70 (14.25)	23.42 (8.56)	29.05 (14.04)	1.52	.23
AUDIT	14.33 (4.38)	14.07 (5.37)	15.57 (5.64)	0.72	.49
BIS Total	68.50 (8.87)	73.33 (10.90)	72.43 (10.47)	1.94	.15
BIS Motor	23.50 (4.35)	25.00 (4.85)	24.77 (5.13)	.85	.43
BIS Attention	18.03 (3.20)	19.17 (2.64)	19.10 (2.77)	1.46	.24
BIS Non Planning	26.97 (4.41)	29.17 (5.21)	28.57 (4.55)	1.73	.18
TRI CEP	25.57 (12.31)	24.37 (10.09)	25.20 (9.47)	0.99	.91
TRI CBC	18.13 (9.99)	16.57 (8.65)	15.63 (7.75)	0.06	.94

Alcohol cons. = average self-reported weekly alcohol consumption in UK units (1 UK unit = 10ml or 8g of pure alcohol); AUDIT = Alcohol Use Disorders Identification Test; BIS = Barratt Impulsivity Scales; TRI = Temptation and Restraint Inventory, CEP = Cognitive and Emotional Preoccupation, CBC = Cognitive Behavioural Control.

Supplementary Table 5.S.2. Self-reported mood and alcohol craving before and after completion of the inhibitory control manipulations, in experiments one and two. Values are means (standard deviations).

	Pre-manipulation			Post-Manipulation		
	Alcohol restraint	Neutral restraint	Disinhibition	Alcohol restraint	Neutral restraint	Disinhibition
A. Experiment one						
AAAQ Inclined	4.46 (1.89)	4.77 (1.60)	4.71 (1.92)	4.17 (2.08)	4.74 (1.78)	4.46 (2.15)
AAAQ Obsessed	0.98 (1.21)	0.80 (1.19)	0.79 (0.93)	0.81 (1.13)	0.98 (1.05)	1.05 (0.97)
AAAQ Resolved	1.15 (1.12)	0.80 (1.12)	1.10 (0.93)	0.92 (1.15)	0.85 (1.37)	1.27 (1.19)
BMIS Pleasant	9.93 (5.84)	8.13 (5.57)	7.73 (6.81)	8.80 (6.74)	6.90 (5.80)	6.23 (6.26)
BMIS Arousal	15.20 (4.08)	15.83 (3.75)	15.30 (2.83)	14.80 (3.47)	14.33 (4.29)	14.93 (3.73)
BMIS Negative	4.13 (2.86)	5.03 (2.72)	5.03 (2.81)	4.20 (2.37)	4.77 (2.33)	5.43 (3.00)
BMIS Positive	8.93 (3.69)	8.73 (3.35)	8.33 (3.33)	8.23 (4.15)	7.30 (4.27)	7.43 (3.34)
B. Experiment two	Alcohol	Neutral		Alcohol	Neutral	
AAAQ Inclined	4.47 (1.75)	5.17 (4.14)		4.17 (1.92)	4.51 (1.90)	
AAAQ Obsessed	1.05 (1.28)	1.20 (1.30)		1.08 (1.40)	1.25 (1.49)	
AAAQ Resolved	1.24 (1.28)	1.45 (1.35)		0.90 (0.96)	1.40 (1.40)	
BMIS Pleasant	8.63 (5.96)	9.13 (5.30)		5.73 (6.68)	9.03 (6.39)	
BMIS Arousal	14.77 (4.31)	15.33 (4.66)		13.10 (4.20)	13.60 (4.09)	
BMIS Negative	4.40 (2.95)	4.33 (2.86)		4.50 (3.04)	3.50 (2.36)	
BMIS Positive	8.40 (3.57)	8.33 (3.82)		6.00 (4.13)	7.63 (4.38)	

BMIS = Brief Mood Introspection Scale; AAAQ = Approach and Avoidance of Alcohol Questionnaire.

Supplementary Table 5.S.3: Participant characteristics in experiment two. Values are means (standard deviations).

<u>Value</u>	Alcohol restraint(N=30)	Neutral restraint (N=30)	t- Value	p-
Gender (M : F)	13 : 17	15 : 15	-	-
Age	21.37 (3.32)	21.00 (2.75)	0.47	.64
Alcohol cons.	30.13 (15.62)	31.18 (23.72)	-0.20	.84
AUDIT	13.97 (5.37)	13.70 (4.26)	0.21	.83
BIS Total	70.03 (10.18)	67.53 (9.79)	0.97	.34
BIS Motor	23.40 (4.78)	23.20 (4.40)	0.17	.87
BIS Attention	18.73 (2.68)	18.37 (2.66)	0.53	.60
BIS Non Planning	27.90 (4.75)	25.97 (4.87)	1.56	.13
TRI CEP	25.70 (10.39)	23.63 (9.27)	0.81	.42
<u>TRI CBC</u>	<u>15.37 (8.18)</u>	<u>16.17 (9.52)</u>	<u>-0.35</u>	<u>.73</u>

Alcohol cons.= average self-reported weekly alcohol consumption in UK units (1 UK unit = 10ml or 8g of pure alcohol); AUDIT = Alcohol Use Disorders Identification Test; BIS = Barratt Impulsivity Scales; TRI = Temptation and Restraint Inventory, CEP = Cognitive and Emotional Preoccupation, CBC = Cognitive Behavioural Control.

Chapter Six

Effects of alcohol cues on craving and *ad-libitum* alcohol consumption in social drinkers: the role of disinhibition.

The results from this experiment have been submitted to The Journal of Experimental Psychopathology. The format, but not content, has been changed to be consistent with the rest of the thesis. At the time of thesis submission a decision on the manuscript has yet to be received.

The roles of the other three authors of the paper version in regards to publication are summarized below:

I designed the study, which was approved by Matt Field (primary supervisor). I collected and analysed the data. I wrote the manuscript. Matt Field, Abi Rose (who took over supervisory duties following retirement of Andrew Goudie) and Jon Cole (member of research group) gave comments on the manuscript before submission and following peer review.

6.1 Abstract

Alcohol cues increase physiological arousal, subjective craving and alcohol consumption. These effects may be mediated by state changes in disinhibition. In this study heavy social drinkers (N=60) were exposed to alcohol cues in a simulated bar environment, or to water cues in a teaching room. Immediately after cue exposure, participants completed a measure of disinhibition (stop-signal task) followed by self-report measures of alcohol craving, and a bogus taste test as a measure of *ad-libitum* alcohol consumption. Alcohol cues had no direct effect on disinhibition although they led to increased subjective craving and alcohol consumption, relative to water cues. Individual differences in disinhibition were associated with self-reported alcohol craving, but not with alcohol consumption, following exposure to alcohol but not water cues. These findings are the first to highlight the association between cue-reactivity and disinhibition in a semi-naturalistic setting.

6.2 Introduction

Individuals who regularly use psychoactive drugs such as alcohol show reactivity to cues associated with drug administration. This reactivity is often seen as increased craving or physiological arousal (Carter and Tiffany, 1999). For example, adolescents dependent on alcohol who are exposed to their alcoholic beverage of choice report increases in subjective craving and salivation (Thomas et al., 2005), and exposure to alcohol advertisements increases alcohol consumption in young adults (Koordeman et al., 2011). Reactivity to drug cues is conventionally explained as a consequence of classical conditioning. Through a history of drug use, stimuli such as sights and smells associated with the substance become conditioned stimuli which can evoke a variety of conditioned responses, ultimately increasing the likelihood of drug self-administration (Rohsenow et al., 1994; Sinha et al., 2011).

While the subjective and physiological effects of cue exposure are well documented (Carter and Tiffany, 1999; Drummond et al., 1990), the effects of cue exposure on psychological processes that are implicated in the development and maintenance of addiction and in relapse among those attempting abstinence, are less well understood. One candidate psychological construct is impulsivity. Impulsivity is a multi-factorial construct consisting of behaviours such as risk taking, sensitivity to immediate reward and disinhibition (Christiansen et al., 2012; Fernie et al., 2010; Reynolds et al., 2006). Cross-sectional research suggests that different facets of impulsivity are elevated in dependent individuals, and are positively correlated with the frequency and quantity of drug use in non-dependent users, such as social drinkers (de Wit, 2009; Lejuez et al., 2010; Verdejo-García et al., 2008).

Until fairly recently, components of impulsivity (including disinhibition) were considered to be relatively stable over time within individuals. More recently, it has been suggested that disinhibition may fluctuate within individuals. For example, de Wit (2009) argued that “abrupt environmental, physiological or emotional events may cause transient ‘state’ changes in either self-control or inhibition that may result in re-initiation of drug use (p28)”. Consistent with this, we provided the first experimental evidence that direct manipulations of disinhibition could influence voluntary alcohol consumption in social drinkers. In two studies, we found that individuals who had been instructed to perform a stop-signal task rapidly, in a

disinhibited fashion, subsequently consumed more alcohol than participants who had been instructed to perform the stop-signal task slowly and cautiously. Furthermore, individual differences in disinhibition were positively correlated with the volume of alcohol consumed, in both studies (Jones et al., 2011a; Jones et al., 2011b).

Furthermore, the presence of alcohol cues leads to temporary increases in disinhibition in alcohol-dependent individuals and social drinkers. Noel and colleagues (2007) found that alcohol-related words presented in the context of a Go/No-go task increased disinhibition in alcoholics. Similarly, Gauggel and colleagues (2010) found increased stop-signal reaction time, a measure of disinhibition, in detoxified alcoholics immediately after they had been instructed to smell alcohol as opposed to water. In social drinkers, Weafer and Fillmore (2012) found that alcohol pictures increased inhibition errors during a Go/No-go task, with similar results shown by Petit and colleagues (2012). Other findings are consistent with the notion of a close link between disinhibition and cue reactivity (Papachristou et al., 2012). However no previous study has examined whether temporary fluctuations in disinhibition caused by exposure to alcohol cues are related to subjective craving and alcohol consumption after cue exposure.

The aims of the present study were; (i) to examine the effects of alcohol cue exposure on disinhibition, craving and alcohol-seeking behaviour in heavy social drinkers, and (ii) examine the relationships between disinhibition, craving and alcohol-seeking following cue exposure. Participants were exposed to either alcohol or neutral cues in a between-groups design, in order to avoid carryover effects of alcohol cues which are problematic when within-subject designs are used (Rohsenow and Niaura, 1999). As cue reactivity is highly context dependent, alcohol cue exposure took place in a simulated bar environment, whereas exposure to neutral cues took place in a neutral environment (Drummond, 2000; Staiger and White, 1988). We hypothesised that exposure to alcohol cues would increase disinhibition, subjective craving, and *ad-lib* alcohol consumption, compared to exposure to neutral cues. We further hypothesised that alcohol cue-induced fluctuations in disinhibition would be associated with cue-induced increases in craving and *ad-lib* alcohol consumption.

6.3 Method

Participants

60 participants (34 female) with a mean age of 21.15 (± 3.30) years took part in the study. Participants were recruited using advertisements placed around the university campus and on the intranet. Participants were informed that they were signing up for a study on taste and olfactory perceptions of different drinks. Inclusion criteria were: heavy drinking according to UK government guidelines (consumption of over 14 UK units per week if female, 21 UK units if male (Edwards, 1996)) with no history of alcohol problems, aged between 18-30 and beer as a preferred alcoholic beverage. All participants provided informed consent before taking part in the study, which was approved by the University of Liverpool Research Ethics committee.

Materials and Equipment

Questionnaires

Urge to drink scales

Urge to drink scales were taken from Kambouropoulos and Staiger (2004). Two statements ‘How much do you want to drink alcohol at this moment for its positive effect?’ (positive urge) and ‘How much do you want to drink alcohol at this moment to take away an unpleasant feeling or mood?’ (negative urge) were presented with 11 anchors ranging from 0 (not at all) to 10 (extremely).

Approach and Avoidance of Alcohol Questionnaire (AAAQ).

The AAAQ (McEvoy et al., 2004) is a 14 item questionnaire in which participants indicate how strongly they agree (0 ‘not at all’ to 8 ‘very strongly’) with statements about drinking ‘right now’. The AAAQ measures self-reported craving on three dimensions: mild inclinations to drink (Inclined / Indulgent), intense inclinations to drink (Obsessed / Compelled) and inclinations to avoid alcohol (Resolved / Regulated).

Brief Mood Inventory Scale (BMIS)

The BMIS (Mayer and Gaschke, 1988) is a 16 item questionnaire in which participants indicate how they feel ‘right now’ in response to various adjectives using a 4 point scale labelled ‘definitely do not feel’, ‘do not feel’, ‘slightly feel’ and ‘definitely feel’. The BMIS measures self-reported mood and arousal states, along four continuums; pleasant-unpleasant, arousal-calm, positive-tired, and negative-relaxed.

Stop-signal task.

The stop-signal task (Logan and Cowan, 1984) was used as a measure of disinhibition. The task was programmed using Inquisit 3.0 (Millisecond Software, 2008) and was presented on a laptop computer. Each trial began with the presentation of a fixation cross (+) for 500ms. Following this, one of two visual ‘go’ stimuli (‘X’ or ‘O’) appeared in the centre of the screen. Participants were required to rapidly categorise these stimuli by pressing a correspondingly labelled key on the keyboard. Seventy five percent of trials were ‘go’ trials; on these trials, the stimulus remained on screen until participants made a response or until a 1500 ms timeout had elapsed. The remaining 25% of trials were ‘stop’ trials. On these trials, an auditory tone occurred at one of four latencies (50 ms, 150 ms, 250 ms or 350 ms) after onset of the visual ‘go’ stimulus. This tone acted as a stop-signal and participants were required to inhibit their response whenever they heard the tone. Before completing the task, participants received standard instructions which emphasised the equal importance of rapid responding to ‘go’ stimuli and successful inhibition of responses whenever they heard the stop-signal. Participants were explicitly instructed not to wait for the stop-signal.

The task was split into four blocks. During an initial practice block of 16 trials (12 go trials, 4 stop trials), participants received feedback after each trial. The practice block was only included to familiarise participants with the task, so data from this block were not analysed. The remaining three blocks were identical and each consisted of 64 trials: 48 go trials and 16 stop trials (four at each stop latency). Trials were presented in a new random order within each block. The task took approximately 15 minutes to complete.

Procedure

Testing sessions took place between the hours of 12pm and 6pm, within the School of Psychology at the University of Liverpool. Participants were randomly allocated to one of two conditions: alcohol cue exposure in a 'simulated bar' (N=30, 17 female) or water cue exposure in a teaching room (N = 30, 17 female). The simulated bar environment was a purpose built laboratory designed to resemble a typical European bar, including beer pumps, posters advertising alcohol and shelves of spirits. The teaching room was approximately the same size and contained only tables and chairs.

Upon arrival participants provided informed consent before being given a questionnaire battery consisting of a two week Timeline Follow-Back diary (Sobell and Sobell, 1992) to measure alcohol consumption in the previous two weeks, followed by the Alcohol Use Disorders Identification Test (Saunders et al., 1993). Participants also completed the Temptation and Restraint Inventory (Collins and Lapp, 1992) and the Barratt Impulsivity Scale v. 11 (Patton et al., 1995). Participants then completed the AAAQ, urge to drink scales, and the BMIS (baseline assessment).

Participants were then taken into their designated laboratory (simulated bar vs. teaching room). They were seated in front of a laptop computer and were told to open either a bottle of beer (Budweiser Budvar, ABV 5%) and pour it into a glass (alcohol cues group) or pour water from a jug into a glass (water cues group). All participants were then instructed to hold the glass in their dominant hand before pressing the space bar on the laptop, which initiated the instructions for cue exposure. The cue exposure procedure was based on Gauggel and colleagues (2010). Instructions required participants to hold the beverage in their drinking hand and think about the temptation to consume the beverage whilst sniffing it. The task consisted of 10 sniffing episodes lasting for 15 seconds each, with a break of 10 seconds between each episode.

Following cue exposure, the glass containing the beverage was removed from sight and both groups of participants were given a second BMIS, AAAQ and urge to drink scales (post-sniffing task assessment). They were also given post-task feedback questionnaires taken from Jones and colleagues (2011b), which were a set of adjectives and statements, scored from 0 (not at all) to 7 (extremely), assessing

difficulty, unpleasantness and how much the task required suppression of urges. The BMIS, AAAQ and post-task feedback questionnaires took approximately 5 minutes to complete. Participants then completed the stop-signal task on the laptop computer, before completing the BMIS, AAAQ, urge to drink scales and post task feedback again (post-stop-signal task assessment). Finally, participants completed the bogus taste test procedure. They were presented with 250ml of chilled beer (Budweiser Budvar ABV 5%) and 250ml of chilled fruit juice (J20 orange and passion fruit) in unmarked glasses (drinks were prepared out of sight). Participants were asked to taste and rate these drinks on 10 adjectives including pleasantness, bitterness and fruitiness, and explicitly told they could drink as much or as little as they liked of each drink and take as long as they needed. This methodology has been used in previous experimental studies to unobtrusively quantify alcohol-seeking behaviour (Field and Eastwood, 2005; Jones et al., 2011a, b). The dependent variable in the taste test was beer as a percentage of total fluid consumed. Following the taste test participants were given a funnelled debriefing (based on Jones et al., (2011b)) which assessed participants' awareness of the aims and hypotheses of the study on three levels: overall, stop-signal task, and taste test. Overall awareness was assessed using an open ended question ('What do you think the experiment was about?'). Awareness of the computer task and taste test were assessed using multiple choice questions ('What was the purpose of the computer task?' and 'What was the purpose of the taste test?') with six possible answers, only one of which was correct, for both questions. Participants were then debriefed before being discharged; they received either course credit or £10 as compensation for travel expenses and time.

6.4 Results

Participant characteristics (Table 6.1).

We conducted independent samples t-tests to investigate group differences in demographic characteristics and alcohol use variables. There were no significant differences between the two groups on any of the variables.

Task perceptions (Table 6.2).

Independent samples t-tests were carried out on the post-task feedback questions after both the cue exposure sniffing task and the stop-signal task. The alcohol cues group found the task significantly more difficult ($t(58) = 1.98, p < .05$) and significantly less frustrating ($t(58) = -2.07, p < .05$) compared to the water cues group. There were no significant differences in post-task feedback after the stop-signal task.

Urge to drink scales (Figure 6.1).

Positive and negative urge to drink scales were analysed using a 2 (scale: positive, negative) x 3 (time: baseline, after drink sniffing, after stop-signal Task) repeated-measures ANOVA with a between subjects factor of group. There was a significant time * group interaction ($F(2,116) = 8.85, p < .01$) and also a significant scale * time interaction ($F(2,116) = 3.29, p < .05$).

At baseline groups did not differ on positive ($t(58) = -1.38, p > .10$) or negative ($t(58) = -0.43, p > .10$) urge to drink. Both positive ($t(58) = 3.76, p < .01$) and negative ($t(58) = 3.01, p < .01$) urge increased significantly in the alcohol cue exposure group after drink sniffing. There was no significant increase in the water exposure group for either positive ($t(29) = -0.75, p > .10$) or negative urge ($t(29) = 1.24, p > .10$).

Between drink sniffing and the stop-signal task positive urge declined in the alcohol cue exposure group ($t(29) = -1.94, p < .05$); negative urge did not show a significant reduction ($t(29) = -.803, p > .10$). Again there were no significant changes in either positive ($t(29) = 1.31, p > .10$) or negative ($t(29) = 0.00, p > .10$) urge in the water cue exposure group.

Between group contrasts showed that negative urge was higher after drink sniffing in the alcohol cues group compared to the water cues group ($t(58) = 1.80, p < .05$).

Following the stop-signal task, this contrast was no longer significant ($t(58) = 1.29, p > .10$). There were no significant differences between groups in positive urge after

drink sniffing ($t(58) = 0.92, p > .10$) or after stop-signal task ($t(58) = 0.92, p > .10$).

These findings demonstrate that alcohol cue exposure led to transient increases in both positive and negative alcohol urges, but exposure to water cues did not.

AAAQ (Table 6.3)

Scores on the AAAQ were log transformed to improve distribution. A Scale (3: Inclined, Obsessed, Resolved) x Time (3: baseline, after drink sniffing, after stop-signal Task) repeated measures ANOVA with a between subjects factor of group was performed to assess changes in AAAQ scores over time. There was a significant group * time interaction ($F(2,55)= 9.04, p <.01$) and also a scale * group * time interaction ($F(4,55)= 2.62, p <.05$). Groups did not differ on any of the three craving scales at baseline: Inclined ($t(58)= 1.48, p >.10$), Obsessed ($t(58)= -0.66, p >.10$) or Resolved ($t(58)= 1.01, p >.10$). After drink sniffing in the alcohol cues group there was a significant increase in Inclined ($t(29)= 2.34, p <.05$) and Obsessed ($t(29)= 6.82, p <.01$), but not Resolved ($t(29)= -0.13, p >.10$) subscales. After drink sniffing in the water cues group there was a significant decrease in Inclined following sniffing ($t(29)= 2.06, p <.05$) but no change in Obsessed ($t(29)= -0.15, p >.10$) or Resolved ($t(29)= 1.18, p >.10$) subscales.

Between drink sniffing and the stop-signal task there were significant decreases in both Inclined ($t(29)= 4.11, p <.01$) and Obsessed ($t(29)= 3.35, p <.01$) subscales in the alcohol cue exposure group, with no change in Resolved ($t(29)= 1.33, p >.10$). In the water cue exposure group there was a further decrease in the inclined subscale ($t(29)= 2.38, p <.05$) with no significant changes in the obsessed ($t(29)= 0.08, p >.10$) or resolved ($t(29)= 1.07, p >.10$) subscales.

Between groups contrasts show that following drink sniffing the alcohol cue group scored higher on the Inclined ($t(58)= 3.13, p <.01$) and Obsessed subscales ($t(58)= 2.54, p <.01$). There was no significant difference in the Resolved subscale ($t(58)= 1.38, p >.10$). After the stop-signal task the groups did not differ on any of the three craving subscales: Inclined ($t(58)= 1.61, p >.10$), Obsessed ($t(58)= 1.24, p >.10$) or Resolved ($t(58)= 1.38, p >.10$). These data suggest that following alcohol cue exposure (but not water cue exposure) there was a significant increase in craving, however craving began to decrease following the stop-signal task.

BMIS (Table 6.3)

A Scale (4: Positive, Pleasant, Arousal, Negative) x Time (3: baseline, after drink sniffing, after stop-signal Task) repeated measures ANOVA with a between subjects factor of group was performed to investigate changes in mood. There were main effects of both subscale ($F(3,55)= 101.12, p <.01$) and time ($F(2,56)= 13.36, p <.01$),

and a subscale * time interaction ($F(6,52)= 4.89, p <.01$), with scores on the pleasant-unpleasant, arousal-calm and positive-tired subscales all decreasing following the stop-signal task. However the subscale * time * group interaction ($F(6,52)= 0.59, p >.10$), and the time * group interaction ($F(2,56) = 1.74, p >.10$), were not statistically significant. Therefore, alcohol and water cue exposure did not lead to differential changes in mood.

Stop-signal task (Table 6.4).

SSRT was calculated using the integration method (Logan and Cowan, 1984). Data from one participant in the alcohol cue exposure group were excluded because their stop-signal reaction time (810ms) was an extreme outlier. Contrary to predictions, alcohol and water cue exposure groups did not differ in SSRT ($t(57)= 0.58, p >.10$). Furthermore there were no group differences in the number of inhibition errors, errors on go trials, or reaction times to go cues ($ps >.10$). Inhibitory control was not affected by alcohol cue exposure.

Alcohol consumption (Figure 6.2).

Participants in the alcohol cue exposure group consumed significantly more beer than participants in the neutral cue exposure group ($t(58) = 3.32, p < .01, d = 0.82$). However, the total volume of fluid consumed (beer and juice combined) did not differ between groups (alcohol cue exposure: 170.50 ± 130.75 ml, vs. water cue exposure 150.20 ± 102.10 ml; $t(58)= 0.67, p >.10$). These results suggest that alcohol cue exposure selectively increased voluntary beer consumption, relative to water cue exposure.

Associations between craving, alcohol-seeking and inhibitory control.

Correlations between the three subscales of the AAAQ, positive and negative urge, alcohol consumption, and inhibitory control following cue exposure were performed separately on alcohol cue exposure and water cue exposure groups. There were no significant correlations between craving / urge at baseline and either SSRT or alcohol consumption in either group ($rs < .29, ps > .10$). There were also no significant correlations between craving / urge and SSRT following drink sniffing or after the stop-signal task in the water cue exposure group ($rs < .13, ps > .10$).

In the alcohol cue exposure group there were several significant positive correlations between SSRT and craving following drink sniffing; AAAQ Inclined ($r = .46, p < .05$) and Resolved ($r = .46, p < .05$) and also following the stop-signal task; AAAQ Inclined ($r = .48, p < .01$), ($r = .46, p < .05$) and Resolved ($r = .48, p < .05$). SSRT was also significantly positively correlated with negative urge after drink sniffing ($r = .43, p < .05$) and after the stop-signal task ($r = .57, p < .01$). AAAQ Inclined and Positive urge were generally associated with ad-lib alcohol consumption (r s ranged between .38 to .49, p s $< .05$). However SSRT was not associated with alcohol consumption in neither group. These correlations suggest disinhibition is associated with alcohol craving, but only following exposure to alcohol cues.

6.5 Discussion

Results from this study indicate that alcohol cue exposure led to increased alcohol craving and *ad-libitum* alcohol consumption. Contrary to expectations, alcohol cue exposure did not lead to increased disinhibition. However, disinhibition was associated with craving / urge following exposure to alcohol cues, but not following exposure to water cues.

We failed to replicate previous observations that alcohol cue exposure causes transient increases in disinhibition (Gauggel et al., 2010; Noël et al., 2007; Weafer and Fillmore, 2012). There are a few possible reasons for our failure to replicate these previous findings. Gauggel et al (2010) and Noël et al (2007) examined detoxified alcoholics, and it is likely that alcoholics will have greater increases in disinhibition following cue exposure compared to social drinkers, given that alcoholics show exaggerated cue reactivity overall. Another possibility is that in our study discrete alcohol cues were presented before but not during the stop-signal task, unlike Weafer and Fillmore (2012) who embedded alcohol-related images directly into their task. Therefore it is possible that within non-dependent social drinkers, the effects of cue exposure on disinhibition are very short-lived, and do not persist for very long after exposure to alcohol cues. By contrast, within detoxified alcoholics,

alcohol cues have effects on disinhibition which persist for some time after cue exposure (Gauggel et al., 2010).

We found that alcohol cue exposure led to increased alcohol craving as assessed with the AAAQ and positive and negative urge to drink scales, which is consistent with a large body of literature (Carter and Tiffany, 1999). Furthermore, we observed a large increase in *ad-libitum* alcohol consumption following exposure to alcohol cues, which is consistent with other studies that used different methodologies (e.g. Koordeman et al., (2011). The primary novel finding from our study is the demonstration that the magnitude of subjective craving following alcohol cue exposure (but not water cue exposure) was positively correlated with the degree of disinhibition immediately following cue exposure. This suggests that in alcohol-related contexts (e.g., bars, pubs), individual differences in disinhibition are associated with subjective craving, but this relationship between disinhibition and craving is not seen in other situations. Our results are consistent with other recent studies which have demonstrated important links between disinhibition and cue reactivity (Papachristou et al., 2012). They are also partly consistent with de Wit's (2009) suggestion that state fluctuations in disinhibition may be associated with vulnerability to relapse (on the assumption that elevated craving increases the risk of relapse). However, our failure to demonstrate increased disinhibition immediately following alcohol cue exposure means that further research is required to identify the circumstances under which alcohol cues lead to fluctuations in disinhibition, and to clarify the clinical implications of any such fluctuations.

We acknowledge one methodological feature of our study that may account for our failure to detect increased disinhibition following alcohol cue exposure. We based our methodology on that reported by Gauggel et al. (2010), who found increased disinhibition in abstinent alcoholics following alcohol cue exposure (relative to exposure to water cues). As in the Gauggel et al. (2010) study, we did not take a baseline (before cue exposure) measure of inhibitory control because repeated administration of cognitive control tasks is known to lead to increased disinhibition, which may have masked the effects of alcohol cue exposure (Hagger et al., 2010; Huizenga et al., 2012). Future studies could include a baseline measure of inhibitory control before investigating the effects of cue exposure on disinhibition, in order to control for individual differences. However, in our opinion this is unlikely to explain

our results, Mainz and colleagues (2012) were unable to replicate the effects of alcohol cue exposure on disinhibition in abstinent alcoholics, and Verdejo-Garcia and colleagues (2012) found no effects of craving induction on inhibitory control in opiate users despite measuring inhibitory control both before and after craving induction. When considered alongside the present findings, it seems that the effects of cue exposure on inhibitory control may not be particularly robust, or they may be moderated by (currently unknown) individual differences.

In summary, this study is the first to demonstrate that, within social drinkers, the magnitude of alcohol craving following alcohol cue exposure was significantly positively correlated with disinhibition following cue exposure. However, we did not observe increased disinhibition following exposure to alcohol cues vs. water cues, as we had originally hypothesised, a finding which may be attributed to features of our experimental design or to the population that we studied. Future studies should aim to elucidate the precise conditions under which alcohol cue exposure leads to increases in disinhibition, and the clinical significance of these state fluctuations in disinhibition.

Table 6.1 Participant characteristics between groups. Means (standard deviations).

	Alcohol (N=30)	Water (N=30)	t- Value	p- Value
Gender (M : F)	13 : 17	13 : 17	-	-
Age	20.67 (2.99)	21.63 (3.58)	1.14	.21
Weekly alc cons.	29.29 (13.15)	28.50 (15.63)	0.33	.74
AUDIT	14.23 (4.42)	13.53 (4.66)	0.60	.53
BIS Total	68.97 (10.69)	70.13 (11.44)	0.82	.69
BIS Motor	23.80 (4.51)	23.77 (4.69)	0.03	.98
BIS Attention	18.23 (3.34)	18.80 (3.19)	0.67	.50
BIS Non Planning	26.93 (5.66)	27.57 (5.03)	0.46	.65
TRI CEP	21.30 (6.81)	23.87 (11.53)	1.05	.30
TRI CBC	16.87 (9.88)	17.53 (7.96)	0.29	.78

*significant at .05 alpha level

Weekly alc cons.= average self-reported weekly alcohol consumption in UK units (1 UK unit = 10ml or 8g of pure alcohol); AUDIT = Alcohol Use Disorders Identification Test; BIS = Barratt Impulsivity Scales; TRI = Temptation and Restraint Inventory, CEP = Cognitive and Emotional Preoccupation, CBC = Cognitive Behavioural Control.

Table 6.2 Post-task feedback scales at post-sniffing and post-stop-signal task assessments. Values are Means (SD in brackets)

	Post-sniffing		Post-stop-signal	
	Alcohol	Water	Alcohol	Water
Irritating	2.21 (2.07)	2.63 (1.92)	3.17 (1.89)	3.37 (2.08)
Difficult	1.47 (1.93)	0.67 (1.09)	2.03 (1.66)	2.03 (1.65)
Annoyed	1.87 (2.08)	2.23 (2.16)	2.90 (1.95)	3.50 (1.91)
Fighting an Urge	3.03 (2.11)	2.70 (1.97)	2.21 (2.14)	2.27 (2.39)
Unpleasant	1.57 (1.96)	1.60 (1.71)	1.69 (1.65)	2.47 (2.01)
Frustrating	3.00 (1.97)	3.97 (1.63)	3.72 (1.65)	3.97 (2.08)

Table 6.3. Self-reported mood and alcohol craving, shown separately for Group at baseline, after cue exposure and after the stop-signal task. Values are Means (Standard Deviations)

	Baseline		After drink sniffing		After Stop-signal	
	Alcohol	Water	Alcohol	Water	Alcohol	Water
AAAQ Obsessed	0.89 (1.04)	0.93 (1.09)	2.08 (1.81)	1.02 (1.34)	1.44 (1.52)	1.03 (1.35)
AAAQ Inclined	4.80 (1.71)	4.17 (1.69)	5.47 (1.75)	3.99 (2.05)	4.59 (2.12)	3.75 (2.31)
AAAQ Resolved	1.49 (1.47)	1.15 (1.34)	1.52 (1.43)	1.05 (1.40)	1.43 (1.46)	0.99 (1.40)
BMIS Pleasant	10.00 (5.46)	7.50 (5.88)	10.17 (4.84)	6.20 (5.59)	7.57 (6.64)	4.03 (6.57)
BMIS Arousal	14.45 (3.94)	14.77 (3.34)	14.67 (3.36)	14.53 (3.47)	13.83 (3.68)	13.60 (3.78)
BMIS Negative	3.66 (2.44)	4.83 (2.46)	3.70 (2.31)	51.7 (2.17)	4.10 (3.00)	5.50 (2.76)
BMIS Positive	8.37 (3.99)	7.73 (3.47)	8.93 (3.23)	7.13 (3.66)	7.40 (3.51)	5.63 (3.83)

BMIS = Brief Mood Introspection Scale; AAAQ = Approach and Avoidance of Alcohol Questionnaire.

Table 6.4 Performance on the Stop-signal task, shown separately for Group. Means (standard deviation)

	Alcohol	Water
Reaction time to 'Go' cues (ms)	558.08 (97.67)	545.00 (85.97)
Number of errors on 'Go' trials	1.83 (1.88)	1.20 (2.12)
Number of Inhibition Errors	13.63 (7.98)	12.40 (7.09)
SSRT	261.00 (146.70)	257.27 (93.89)

Figure 6.1. Positive and negative urge over time. Values are mean \pm SEM

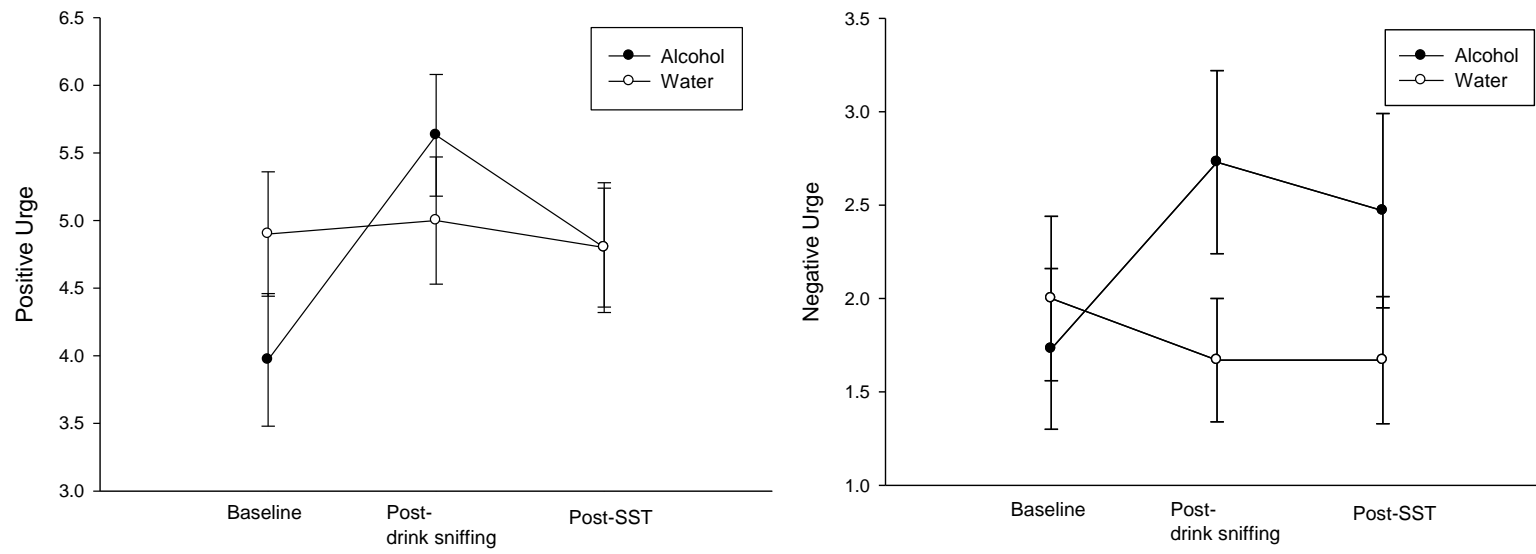
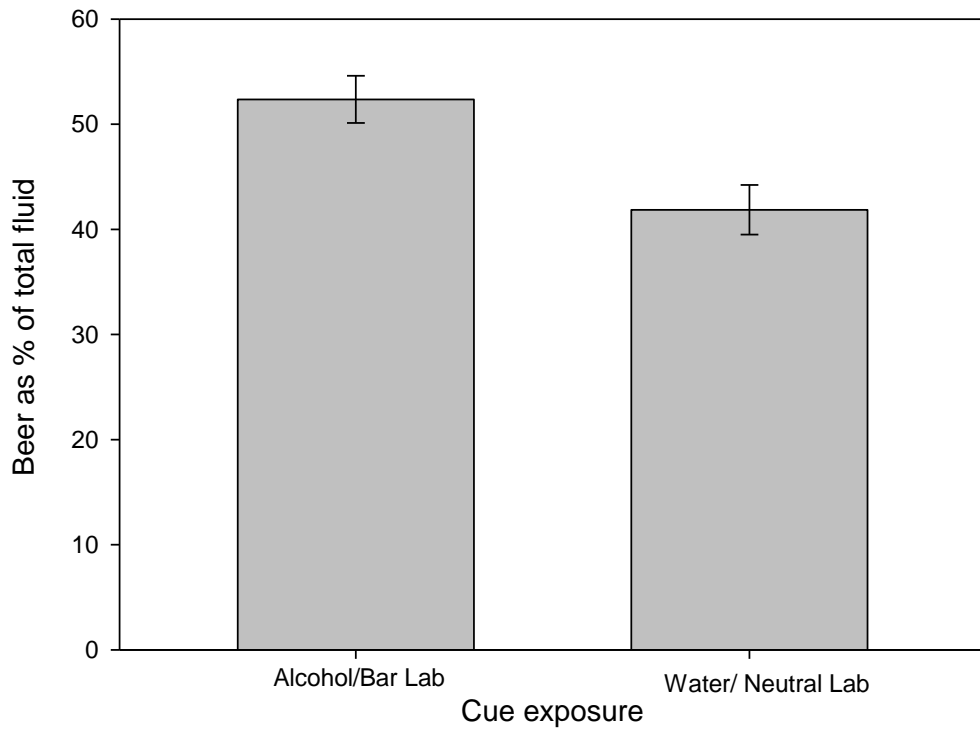


Figure 6.2. Alcohol consumption during the taste test. Values are mean \pm SEM



Chapter Seven

The effect of restraint beliefs on alcohol-seeking behaviour

This experiment was designed to examine whether beliefs about alcohol-restraint could be manipulated in a similar way disinhibited behaviour could be. Following a modified stop-signal and Implicit Association Task individuals were given bogus feedback, suggesting they had 'high restraint' or 'low restraint' before the bogus taste test.

The results from this experiment were published in *Psychology of Addictive Behaviours* (Vol 26(2), pages 325-329), as a brief report. The review process requested we reduced procedural details and remove tables reporting self-report data. The format, but not content, has been changed to be consistent with the rest of the thesis.

The roles of the other three authors of the paper version in regards to publication are summarized below:

I designed the study, which was approved by Matt Field (primary supervisor). I collected and analysed the data. I wrote the manuscript. Matt Field, Andrew Goudie (at the time was a secondary supervisor) and Jon Cole (member of research group) gave comments on the manuscript before submission and following peer review.

7.1 Abstract

Individuals who believe that they have high levels of restraint over motivated behaviours such as cigarette smoking are, paradoxically, more likely to engage in those behaviours when tempted (Nordgren et al., 2009). Our aim was to experimentally manipulate heavy drinkers' beliefs about their drinking restraint, in order to examine the effect on drinking behaviour. Sixty heavy drinkers completed an implicit association test (IAT) and a stop-signal task before receiving bogus feedback on their task performance which indicated that they had either high or low levels of drinking restraint. Participants then completed a bogus taste test in which they were able to consume beer and a soft drink. Results indicated that the group that were falsely led to believe that they had a high level of drinking restraint subsequently consumed more beer than the group that had been led to believe that they had a low level of drinking restraint. This study demonstrates that beliefs about drinking restraint can influence drinking behaviour, in that individuals who overestimate their control over drinking are at greater risk of drinking to excess when exposed to tempting situations.

7.2 Introduction

The role of drinking restraint in the transitions from social drinking to alcohol dependence, and from dependence to recovery, has been intensively studied. Restrained drinkers have been defined as those who are “cognitively and behaviourally pre-occupied with controlling their (alcohol) intake” (Collins and Lapp, 1992, p625). While many alcohol treatment programmes aim to increase patients’ motivation to limit their alcohol intake (Miller 1996) and their confidence in their ability to abstain (self-efficacy; Larimer, Palmer and Marlatt, 1999), studies of the relationship between drinking restraint and heavy drinking in non-dependent populations have yielded some counterintuitive findings. For example, a series of laboratory and field studies have revealed that restrained drinkers tend to drink more, not less, than drinkers with low scores on measures of drinking restraint (Collins, 1991; Collins and Lapp 1993; Muraven, Collins, Morsheimer, Shiffman and Paty 2005a; 2005b). Collins (1993) introduced the limit violation effect (LVE) as a conceptual framework to understand these effects of drinking restraint. In essence, restrained drinkers impose limits on their future alcohol consumption, but drinking in excess of those limits is attributed to personal failings, which leads to negative mood, which in turn leads to further increases in drinking in order to cope with this negative mood. Results from field studies have generally been consistent with this framework, as individuals who violate self-imposed drinking limits tend to drink more on subsequent days, particularly if those individuals score highly on self-report measures of drinking restraint (Muraven et al., 2005a; 2005b). On the other hand, laboratory studies in which limit violations were experimentally manipulated show that highly restrained drinkers tend to drink less, not more, immediately after a limit violation (Collins, 1993; Collins et al., 1994).

The literature on drinking restraint relates to individual differences in the *motivation* to limit drinking. However, this literature does not directly address the potential role of individual *beliefs* about the ability to limit drinking. While it is generally accepted that high levels of self-efficacy (confidence in the ability to abstain) are protective against future relapse, a recent meta-analysis suggests that the relationship between self-efficacy and subsequent relapse in tobacco smokers is actually rather weak

(Gwaltney et al. 2009). Indeed, extremely high self-efficacy may even be associated with an increased risk of subsequent relapse, perhaps reflective of overconfidence (Staring and Breteler 2004). Recently Nordgren, Van Harreveld and Van Den Pligt., (2009) conducted an experimental study that relates to this issue. The authors predicted that smokers who *believe* that they are able to limit their smoking behaviour would over-expose themselves to tempting situations, and as a consequence they would be more likely to succumb to temptation (i.e., smoke cigarettes). Nordgren et al. (2009; Study 3) manipulated self-control beliefs in cigarette smokers, by requiring participants to complete a smoking-related implicit association test (IAT) before being provided with bogus feedback based on their performance on the task. Regardless of their actual IAT performance, participants were randomly allocated to receive bogus feedback indicating that they had either high or low levels of smoking restraint. After receiving this bogus feedback, participants were able to choose the level of temptation to which they were prepared to be exposed while being offered a financial incentive for overcoming the temptation to smoke. The primary finding was that the group who were informed that they had high levels of smoking restraint exposed themselves to more temptation, and were more likely to smoke as a consequence (despite the financial incentive to abstain), compared to smokers who had been informed that they had low levels of smoking restraint. Nordgren et al., (2009) argued that this ‘restraint bias’ may be one reason why smokers relapse to smoking after a period of abstinence: they have unrealistic *beliefs* that they will be able to resist temptation, and thus expose themselves to high-risk situations in the future.

In the present study, our primary aim was to examine whether a similar ‘restraint bias’ would influence alcohol-seeking behaviour in heavy social drinkers. To recap, previous work on drinking restraint suggests that high levels of restraint are associated with heavy drinking, and work on restraint beliefs and self-efficacy suggests that very high restraint beliefs, or over-confidence, may also increase the risk of relapse to smoking. One explanation of these findings is that high levels of drinking restraint (the *motivation* to limit drinking) and *beliefs* in the ability to limit drinking may both increase the risk of heavy drinking. However, this explanation is speculative given that the effect of restraint beliefs on drinking behaviour (rather than smoking) has not yet been investigated. In the present study, we adapted the

methodology described by Nordgren et al. (2009) in order to examine if the effects of providing bogus feedback regarding drinking restraint would influence subsequent drinking behaviour. Our primary prediction was that individuals who were (falsely) informed that they had a high level of drinking restraint would subsequently consume more alcohol than individuals who were falsely informed that they had a low level of drinking restraint. We also investigated self-reported mood and alcohol craving in response to the bogus feedback, in order to investigate if changes in these variables could account for the anticipated effects of bogus feedback on drinking behaviour.

7.3 Method

Participants

Sixty heavy social drinkers (34 Female) were recruited via online and poster advertisements from the staff and students at the University of Liverpool. Heavy drinking was defined as alcohol consumption in excess of UK government guidelines (14 units per week for females, 21 units for males; 1 unit = 8g alcohol (Edwards 1996)). We recruited heavy social drinkers as this population should exhibit some degree of drinking restraint and temptation to drink, whereas light social drinkers should not be preoccupied with controlling their alcohol intake. Additional inclusion criteria were: aged between 18 and 30, no history of alcohol dependence or problems, and a liking for both beer and fruit juice. All participants provided informed consent before taking part in the study, which was approved by the University of Liverpool Research Ethics Committee.

Materials

Implicit Association Test (Greenwald et al. 1998). This task was programmed in Inquisit 2.0 (Millisecond Software, 2002). Full details are available on request from the authors, but in brief this is a reaction time paradigm, which is used to assess the strength of associations between alcohol-related and neutral stimuli, and positively

and negatively valenced words (e.g. see Wiers, Van Woerden, Smulders, and De Jong., 2002). The task took approximately ten minutes to complete.

Stop-signal task (Logan and Cowan 1984): This task was programmed in Inquisit 2.0 (Millisecond Software, 2002). In this task, participants were required to make a rapid manual response to visually presented ‘Go’ stimuli, but to inhibit their response whenever they hear an auditory ‘Stop’ signal. Full details are available on request from the authors, but in brief participants were required to rapidly categorise ‘Go’ stimuli, but to inhibit their response on 50% of trials when an auditory ‘stop’ tone was presented. This task took approximately 10 minutes to complete.

Procedure

All testing took place in laboratories in the School of Psychology, University of Liverpool between 12pm and 6pm. Testing sessions lasted around 35 minutes. Participants were randomly allocated to either ‘high restraint’ or ‘low restraint’ groups at the beginning of the study. Participants were explicitly informed that the study was an investigation of the relationship between self-control and taste perception. Participants initially completed a questionnaire battery comprising a retrospective two-week Timeline Follow-Back alcohol diary (Sobell and Sobell 1992) to obtain an estimate of average weekly alcohol consumption, the Alcohol Use Disorders Identification Test (AUDIT) (Saunders et al. 1993), the Barratt Impulsivity Scale (BIS) (Patton et al. 1995), a trait measure of impulsivity, and the Temptation and Restraint Inventory (TRI) (Collins and Lapp, 1992) to identify individual differences in drinking restraint.

Participants were then informed that they would be completing two computer tasks, the purpose of which was to assess their ability to control their alcohol consumption. All participants then completed the IAT followed by the Stop-signal task, before two bogus feedback screens were presented. For participants who had been randomly allocated to the high restraint group, the IAT score was positive (142 milliseconds); for participants who had been allocated to the low restraint group, the IAT score was negative (-169 milliseconds). Feedback for the Stop-signal task was provided in the form of a ‘Behavioural Control Capacity Index’: participants in the high restraint group were given bogus feedback indicating a higher score on this index than participants in the low restraint group (76.6 vs. 39.8). Participants completed an IAT

for consistency with Nordgren et al. (2009), and we added the stop-signal task as the task has high face validity as a measure of self-control; we reasoned that bogus feedback about drinking restraint should be more credible if that feedback was based on performance on two tasks rather than a single task. In order to further increase the effectiveness of the bogus feedback, the experimenter clearly wrote down the feedback values for both the IAT and Stop-signal tasks, before showing the participant histograms which ostensibly showed the distribution of these values in the general population, and their relationship to ability to control alcohol consumption. For participants in the high restraint group, their values placed them in the top quartile for both tasks, and the experimenter explained that this indicated that this meant that they had very good ability to control their alcohol consumption. For participants in the low restraint group, their values placed them in the bottom quartile for both tasks, and the experimenter explained that this indicated that they had very poor ability to control their alcohol consumption.

Participants then completed a manipulation check, which comprised a single item scale: 'How would you rate your ability to control your alcohol consumption?' with 9 anchors ranging from 0 (extremely poor) to 8 (extremely good). Participants then completed the Brief Mood Introspection Scale (BMIS), a measure of self reported mood and arousal (Mayer and Gaschke 1988) and the Approach and Avoidance of Alcohol Questionnaire (McEvoy et al. 2004), which yields scores on three components of alcohol craving: Inclined / Indulgent (corresponding to mild craving), Obsessed / Compelled (corresponding to strong craving) and Resolved / Regulated (corresponding to desires to limit alcohol consumption). Participants then completed the bogus taste test. They were provided with 250ml of chilled beer (Kronenbourg 1664, 5.0% ABV) and 250ml of chilled fruit juice (apple and mango 'J²0') in unmarked glasses. They were asked to taste the drinks and rate them on a variety of dimensions (e.g. pleasant, bitter, fruity). Participants were given as much time as they wished to complete the taste test. No participant took more than five minutes to complete the taste ratings, although we did not record the time elapsed before participants indicated that they had finished. This bogus taste test procedure, modified from a paradigm originally described by Marlatt et al (1973), is sensitive to experimental manipulations of the motivation to drink alcohol (Jones et al. 2011a; Field and Eastwood, 2005). Finally, participants completed a funnelled debriefing

questionnaire, which assessed their awareness of the aims and hypotheses of the study (based on Jones et al. 2011b).

7.4 Results

Baseline characteristics (Table 7.1)

Differences between the two experimental groups were assessed using independent groups t-tests. Participant age and weekly alcohol consumption were log transformed before analysis to improve their distributions. There were significant group differences on the attentional impulsiveness subscale of the BIS ($t(58) = -2.44, p = .02$) and the cognitive and emotional preoccupation subscale of the TRI ($t(58) = -2.40, p = .02$), with the low restraint group scoring higher on both. Given these group differences, both of these variables were included as covariates in subsequent analyses, in order to statistically control for their influence on the primary variables of interest.

Performance on the IAT and Stop-Signal task.

We did not anticipate any group differences in these measures, given that bogus feedback was provided after participants had completed the tasks. Group differences were analysed using univariate Analysis of Covariance (ANCOVA), with group as a between-subjects factor and BIS attention and TRI CEP as covariates. There were no significant group differences in IAT scores ($F(1,56) = 1.06, p = .31$) or the number of inhibition errors ($F(1,56) = 3.74, p = .06$). Data are not shown. Given the non-significant trend for group differences in inhibition errors, this was included as an additional covariate in all subsequent analyses.

Manipulation check

Post-manipulation drinking restraint beliefs were analysed using a univariate Analysis of Covariance (ANCOVA), with a between subjects factor of group and BIS attention, TRI CEP and inhibition errors as covariates. The main effect of group was statistically significant ($F(1,55) = 13.11, p < .01$) with the high restraint group

scoring higher (5.31, SD = 1.07) than the low restraint group (4.07, SD = 1.08). This suggests the experimental manipulation was successful, in that the low restraint group believed they had less ability to control their alcohol consumption than the high restraint group.

Self reported craving and mood.

Mean scores on the three AAAQ subscales, and four BMIS subscales were analysed using two separate univariate ANCOVAs both with a between-subjects factor of group, and BIS attention, TRI CEP and inhibition errors as covariates. There were no significant differences between groups on any of the subscales for either the AAAQ (Inclined ($F(1,56)= 0.32, p= .53$), Obsessed ($F(1,56)= 1.42, p= .24$) or Resolved ($F(1,56)= 1.83, p =.18$)) or BMIS (pleasant ($F(1,56) =0.68, p =.41$), arousal ($F(1,56)= 0.14, p =.71$), positive ($F(1,56)=0.89, p =.35$) and negative ($F(1,56)= 0.34, p= .56$)) subscales. These results suggest that the manipulation did not lead to any group differences in subjective alcohol craving or mood.

Bogus taste test (Figure 7.1.)

Beer consumption (as a percentage of total fluid consumed) was analysed using a univariate analysis of covariance, with a between-subjects factor of group, and BIS attention, TRI CEP and inhibition errors as covariates. This revealed a significant main effect of group ($F(1,56)= 5.17, p =.03$, Cohen's $d=.60$). The high restraint group consumed more beer than the low restraint group, as predicted. Additional analyses revealed that there were no significant group differences in consumption of either fruit juice ($F(1,55) = 0.96, p =.33$), or total fluid ($F(1,55)= 0.02, p=.89$), which suggests that the effects of the experimental manipulation were specific to beer consumption.

Supplementary Analysis: Awareness

Eight participants (3 from the high restraint group, 5 from the low restraint group) were classified as aware of the purpose of the computer tasks, i.e. to manipulate beliefs about control over alcohol consumption. A larger number of participants (20; 10 from each group) were aware of the purpose of the taste test, i.e. to measure alcohol-seeking behaviour. Finally, three participants (one from the high restraint group, two from the low restraint group) were classified as aware of the overall

purpose of the experiment (i.e., to manipulate beliefs about control over alcohol consumption before examining effects on alcohol-seeking behaviour). We repeated the analysis of beer consumption data after removing participants who were classified as aware of these different aspects of the study (in three separate analyses). In all cases, removal of these participants did not affect the result, i.e. the group difference in beer consumption remained statistically significant.

7.5 Discussion

Results from this study demonstrated that participants who were given bogus feedback suggesting they had a high level of drinking restraint consumed significantly more alcohol during a bogus taste test than those who believed they had a low level of drinking restraint. Furthermore, additional analyses suggest that the bogus feedback did not alter mood or alcohol craving, and the effects on alcohol consumption could not be attributed to demand effects. This study is therefore the first to demonstrate that priming differential levels of drinking restraint beliefs can contribute to drinking behaviour among heavy social drinkers.

The primary finding demonstrates that heavy drinkers who believe they have high drinking restraint will consume more alcohol than those who believe they have low drinking restraint, when placed in a context that promotes ad-lib drinking. When applied to a real life setting, these results suggest that individuals who overestimate their degree of drinking restraint (or control over drinking) may be more likely to relapse, or consume greater amounts of alcohol. Our results extend those described by Nordgren et al. (2009) into the domain of alcohol use, although one important difference between the two studies is that in our study our participants did not choose the level of temptation that they were prepared to expose themselves to, unlike in the Nordgren et al. (2009) study. Nonetheless, both studies demonstrate that participants who believe that they have a high level of restraint over their drinking or smoking behaviour are more likely to expose themselves to temptation (Nordgren et al., 2009), or consume more of the substance (the present study), compared to participants who believe that they have a low level of restraint. We also included self

report measures of craving and mood in order to assess whether the bogus feedback would influence these variables. Analyses revealed no significant group differences in either craving or mood, which suggests that these variables were not sensitive to the bogus feedback.

At first glance these results (and those reported by Nordgren et al., 2009) may appear surprising when one considers that effective restraint (as opposed to disinhibited behaviour) are protective against substance abuse and addiction as revealed by a large body of cross-sectional (Verdejo-García et al. 2008), longitudinal (Wong et al. 2006) and experimental (Jones et al., 2011a; 2011b) research. It is important to contrast this aspect of restraint – restraint *ability* - with the *motivation* to limit drinking (cf. Collins, 1993) and *beliefs* about the ability to limit drinking, both of which may paradoxically increase substance use and relapse after a period of abstinence. Our results also raise a number of issues that could be investigated in future research. Firstly, we did not include a control group of participants who did not receive any feedback about their level of drinking restraint. Future studies should include control group comparisons, in order to investigate whether high restraint beliefs lead to an increase in drinking behaviour, or low restraint beliefs lead to a decrease in drinking behaviour, or if both processes are in operation. Future studies should also investigate the psychological mechanisms that underlie the effects reported here (for example, overconfidence or unrealistic beliefs in the ability to restrict drinking leading to an increase in drinking behaviour similar to the effects seen in smokers (Staring and Breteler 2004), as clarification of these issues may lead to useful clinical applications of this research. Finally, although we recorded the amount of alcohol that participants consumed, we did not measure the time that participants took to complete the taste test procedure, so one question for future research is whether restraint beliefs influence the rate of alcohol consumption in addition to the amount consumed.

To summarise, in this novel experimental study we examined the effects of priming beliefs about drinking restraint on alcohol-seeking behaviour. The results demonstrate that beliefs about drinking restraint can influence alcohol consumption, with those who believed they had high levels of drinking restraint consuming more alcohol than those who believed that they had low levels of drinking restraint.

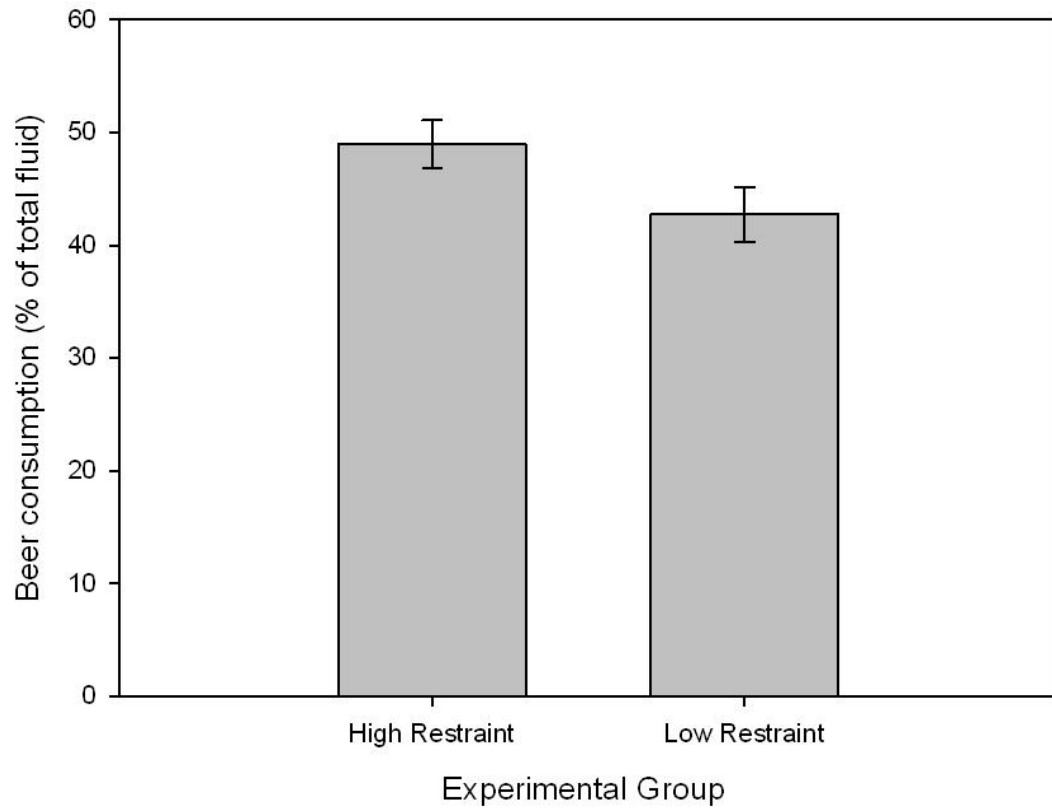
Table 7.1: Characteristics of participants allocated to high and low restraint groups. Values are means (standard deviations in brackets).

	High restraint (N=30)	Low restraint (N=30)	t- Value	p- Value
Gender (M : F)	13 : 17	13 : 17	-	-
Age	20.63 (2.66)	20.66 (2.68)	-0.05	.96
Alcohol consumption	71.10 (47.05)	58.87 (24.67)	0.68	.50
AUDIT	13.27 (5.26)	15.67 (5.01)	-1.81	.08
BIS Motor	23.33 (3.47)	24.47 (4.86)	-1.04	.30
BIS Attention	17.67 (2.14)	19.53 (3.60)	-2.44	.02*
BIS Non Planning	26.03 (5.03)	26.80 (5.30)	-0.58	.57
TRI CEP	22.33 (9.39)	28.53 (10.57)	-2.40	.02*
TRI CBC	16.50 (7.09)	18.83 (7.79)	-1.21	.23

* $p < .05$

Alcohol consumption = average self-reported weekly alcohol consumption in UK units (1 UK unit = 10ml or 8g of pure alcohol); AUDIT = Alcohol Use Disorders Identification Test; BIS = Barratt Impulsivity Scales; TRI = Temptation and Restraint Inventory, CEP = Cognitive and Emotional Preoccupation, CBC = Cognitive Behavioural Control.

Figure 7.1: Group differences in beer consumption (as a percentage of total fluid consumed) during the bogus taste test. Values are mean \pm SEM



8. General discussion

The main aim of this thesis was to explore the causal relationship between (dis)inhibition and alcohol consumption in heavy social drinkers, using experimental manipulations. In Chapter One the theoretical evidence supporting the link between disinhibition and drug/alcohol use was discussed in terms of behavioural associations and possible avenues of causality. The examination of the evidence base revealed two unresolved issues: i) does disinhibition function as a state, and fluctuate within individuals, and ii) are social drinkers more likely to drink to excess when in a disinhibited state. These research questions were investigated in heavy drinking young adults (the majority of whom were university students), as these individuals often fit the criteria for alcohol abuse and are at a high risk for going on to develop alcohol dependence in later life. The research questions were in need of investigation for two reasons; firstly, to increase our theoretical knowledge of addiction, specifically individual processes which may contribute to alcohol use, and secondly, if the causal role was identified then disinhibition can be targeted as a potential treatment possibility. As well as the main hypothesis I also drew influences from major theoretical models, in order to strengthen the claims made by this research. By examining established factors that influence alcohol consumption, such as trait impulsivity and craving, but also factors hypothesised to influence alcohol consumption such as motivations to drink and beliefs about restraint, it was possible to examine the role of disinhibition on alcohol-seeking in relative isolation from these potential confounding factors.

8.1 Summary of main findings

8.1.1 Behavioural disinhibition

In the first experimental chapter (Chapter Three), I set out to provide an extension to a project completed prior to undertaking the thesis (see Jones et al., 2011a). The between subjects design involved three experimental groups who were given different instructions on how to complete a stop-signal task in order to induce

specific motivational biases. In accordance with the previous experiment, we termed these motivational biases as subtle changes in mental sets, i.e. a bias on fast responding at the expense of inhibition was a ‘disinhibited’ mental set, whereas a bias on inhibition over fast responding was termed a ‘restrained’ mental set. The third comparison/control group was included (performing the stop-signal task with equal emphasis on inhibition and fast responding, or a ‘neutral’ mental set) so that it was possible to identify which bias or mental set, if any, contributed to the group differences in alcohol-seeking. It was of theoretical importance to establish whether disinhibited responding led to increased alcohol consumption, whether restrained responding led to decreased alcohol consumption or whether both biases exerted independent effects. The results demonstrated that it was the restrained group that exhibited reductions in alcohol consumption, in comparison to the neutral group (of equal motivation) and the disinhibited responding group. This demonstration, that restraint may be protective against alcohol consumption, augmented the evidence for causality initially presented by Jones et al., (2011a). Furthermore, it supported comparable research on self-control regulation reducing health risk behaviours (e.g. smoking: Muraven et al., 2010).

The results of this experiment, when considered alongside Jones et al. (2011a) and Guerrieri et al., (2009), also served to highlight similarities in the basic cognitive and behavioural processes that underlie diverse, motivated behaviours. These studies offer support to the general theoretical models of impulsivity in relation to alcohol (ab)use and obesity (Dawe and Loxton 2004; Lubman et al. 2004), which imply inhibitory control deficits are a risk factor for ‘loss of control’ over motivated, appetitive behaviours. In relation to this, recent work has emerged to show that cautious responding, primed using a similar methodology on the stop-signal task, can serve to reduce risk taking behaviour (Verbruggen et al. 2012), which, in turn, is related to increased alcohol use (Ferne et al. 2010). Interestingly, Verbruggen and colleagues found that after one brief session of restrained responding risk aversive decision making was reduced up to 2 hours later, indicative again of causality, but also demonstrating that these effects may have some longevity.

Experiment one also served to clarify the role of processes such as motivation, (assessed by the Temptation and Restraint Inventory) and mood/arousal, (assessed with both self-report and physiological measures). The latter was considered a

possible confounding factor in the initial experiment (Jones et al., 2011a), in that increased number of inhibition errors in the 'disinhibition' group may have increased negative mood and/or arousal, which may have been the mechanism behind increased alcohol consumption (Willner et al. 1998). However, the lack of group differences in mood/arousal suggests this was not the case here. Another limitation of Jones et al., (2011a) was that non-alcoholic beer was used during the bogus taste test, which was originally included to examine the effect of inhibition manipulations not confounded by the pharmacological effects of alcohol (de Wit 1996; Rose and Duka 2007) (e.g. any fluctuations in disinhibition, may be nullified by an alcohol prime). However, the use of alcoholic beer in Chapter Three allows a discounting of this possibility. Finally, I assessed whether social desirability may have influenced participants' behaviour by using a funnelled debriefing, however, I found no social desirability effects.

In the second experiment (Chapter Four), I attempted to examine in more depth the effect of the mental sets discussed above, specifically on biological markers of (dis)inhibition (the Inhibition P300). The rationale for this was to examine if and how experimental manipulations of motivational bias were influencing the neuropsychophysiological inhibition processes, as evidence suggests ERPs are more sensitive measures of (dis)inhibition (Luijten et al. 2011). In this study I used a within subjects design, with two conditions (the emphasis on restraint versus normal responding). A within subjects design was employed as more robust conclusions about fluctuations in disinhibition could be drawn from examining the effects of motivational bias within subjects. Again, what was found was a significant effect on behaviour. When performing under restraint instructions, participants exhibited a reduced number of inhibition errors and slower reaction times on the stop-signal task compared to participants who had no motivational bias (normal response conflict). Furthermore, there were significant differences in the neuropsychophysiological component underlying inhibition (P300), reinforcing the motivation to respond with caution, which led to reduced conflict on the task. I also demonstrated that the inhibition P300 neuropsychophysiological component was associated with alcohol-seeking and disinhibition under response conflict.

The evidence from Chapters Three and Four suggested that a specific motivational bias to restrain can lead to reductions in response conflict. I also found that these

alterations in response conflict/motivational bias influenced alcohol-seeking (specifically in Chapter Three). These findings are partly consistent with similar research suggesting conflict, brought about by cognitive load, may be detrimental to executive control (Verbruggen et al. 2012). These were some of the first studies to examine whether disinhibition, measured behaviourally using response inhibition tasks, could fluctuate in sober individuals and possibly play a causal role in alcohol-seeking behaviour.

Following the publication of Jones et al., (2011a), Houben and colleagues (2011a) argued that,

‘whilst priming such a mental state is interesting to show causality, it is highly unlikely that temporarily priming an inhibitory mental state induces long-term effects on both inhibitory control and drinking behaviour (p.132-133)’.

Subsequently, they followed up these ideas by examining whether ‘training’ inhibition specifically to alcohol cues could influence alcohol-seeking and if the effects would be longer lasting. The rationale for this is grounded in the emerging evidence that alcohol cues may cause transient increases in disinhibition in both clinical and non-clinical samples (Gauggel et al. 2010; Noël et al. 2007; Petit et al. 2012), but also that inhibiting responses to specific stimuli can cause changes in affective evaluations of these stimuli (Buttaccio and Hahn 2010), specifically, making them more negative (Veling et al. 2008).

However, Houben and colleagues’ manipulation, a modified Go/No-go task, was unsuitable to assess whether cue-specific inhibition training causes state changes in (dis)inhibition. Furthermore, they focused their analysis on changes in affective evaluations of alcohol (discussed in Chapter 5.9). They did attempt to measure post task disinhibition using a modified stop-signal task, however, this may be unreliable due to the fundamental differences in the tasks (i.e. action cancellation versus action restraint: see Chapter 1.4.2). Therefore, in Chapter Five (Experiment One), I designed an experiment that built upon the previous research in this thesis and also the critique from Houben and colleagues. Using a modified stop-signal task, I examined whether inhibition could be trained to be ‘cue-specific’. I also sought to examine the claim that training inhibition to alcohol cues, rather than priming a restrained/disinhibited mindset, would translate to reduced alcohol consumption

outside the laboratory. Therefore, I measured alcohol consumption at a week long follow up, as well as immediately following the manipulation (similar to the studies of Houben and colleagues 2011a; 2012).

The results of this experiment demonstrated that if alcohol cues signalled a high probability of requiring an inhibitory response (90% chance), then inhibition became progressively more successful to these cues. This led to decreases in inhibition errors from the first block to the third, and also to an increase in reaction times when participants were required to respond to alcohol cues (10% chance). These increases in reaction times were likely to be the result of an anticipation to inhibit. In this study I included two comparison conditions - a group who were trained to inhibit to neutral cues and respond to alcohol cues (Neutral restraint), and a group who received equal exposure to alcohol and neutral cues with no inhibition (disinhibition). The disinhibition group was included for two reasons; i) In both of Houben and colleagues' experiments (2011a;2012) it was unknown whether training inhibition specifically to alcohol cues reduced alcohol consumption and affective associations, or that training fast responding to these cues increased consumption and affective associations, and ii) in Chapter Three, I suggested that disinhibition priming could be more potent if participants did not have to inhibit at all (rather than reducing the emphasis on inhibition). The disinhibited group would also serve to examine what possible mechanism could be in effect. Specifically, if the limited resource model is indeed a robust phenomenon, then even if inhibition is being trained to alcohol and neutral cues, the limited pool of self-control resources will be depleted (assuming response inhibition causes ego depletion, see Huizenga et al. 2012). Alternatively, if devaluation of alcohol stimuli is the mechanism then it may be that be this group would consume the most alcohol, as their affective associations with alcohol will be strengthened the most (Veling et al. 2008).

The results of this manipulation not only demonstrated observable 'cue-specific training' to both alcohol and neutral cues, but also led to group differences in alcohol consumption immediately following the training. Individuals who were trained to inhibit specifically to alcohol cues had reduced alcohol consumption in comparison with those trained to inhibit to neutral cues, and those who responded quickly with no inhibition. There was no significant difference in alcohol consumption between the neutral training and disinhibited (no inhibition) group. Again, this study provides

support for the hypothesis that disinhibition may play a causal role in alcohol consumption (de Wit 2009). However, I tentatively argue that it did not support any effects of the limited resource models as the disinhibited group did not show reductions in alcohol-seeking, compared to groups who had exerted self-control prior to consumption. One possible explanation for this be that individuals were not actively motivated to limit their alcohol consumption in this case (cf. Christiansen et al. 2012).

In Chapter Five (Experiment One) the reductions in alcohol-seeking were not evident outside the laboratory, as there was no significant group differences in alcohol consumption at a weeklong follow up. Whilst this finding did not support previous research (suggesting one session training can influence drinking outside the laboratory (Houben et al., 2011a; 2012)), it is probably not surprising considering Houben and colleagues did not train response inhibition *per se*, rather, affective associations. It is likely, given the nature of (dis)inhibition, that one training session is not potent enough, or that inhibitory control needs to be trained specifically in alcohol consumption environments. Also, whilst it is possible the Alcohol Restraint group may have reduced affective associations (Houben et al 2011a; 2012), the fact the disinhibition group did not drink the most alcohol immediately following the manipulation suggests that inhibition training is a mechanism of effect demonstrated in Chapter Five (Experiment One). However, this interpretation is tentative given that no measure of affective associations was taken, as this was not the primary aim.

If we consider the findings of Chapters Three and Five (Experiment One), it seems that training inhibition to alcohol cues has similar effects on alcohol-seeking to inducing a restrained mindset. Unfortunately, it is difficult to assess these results side-by-side (although this could be an interesting avenue for future research). A rudimentary examination would be to compare the size of the effect on alcohol consumption in each experiment (using Cohen's d). Using non-specific motivational biases, the effect size of alcohol consumption between the 'Restrained' group and 'Neutral' group was $d = .27$, whereas using cue-specific (behavioural) training the effect size of alcohol consumption between the 'Alcohol Restrained' group and the 'Neutral Restrained' group was $d = .86$. A similar pattern emerged when comparisons were between the '(Alcohol) Restrained' and 'Disinhibited' groups, with an effect size of $d = .56$ in Chapter Three and $d = .65$ in Chapter 5 (Experiment One). These

resulting effect sizes suggest that training inhibition directly to alcohol cues may provide greater reductions in alcohol-seeking than inducing non-specific mindsets. Interestingly, research into calorie consumption has attempted to utilise non-specific inhibition training by gradually increasing / decreasing the difficulty of the stop-signal task over time (Guerrieri et al. 2012). Thus, it remains to be seen whether a similar non-specific manipulation will translate to comparative changes in alcohol consumption.

As well as directly manipulating inhibitory control, this thesis set out to examine whether external factors, in this case cue exposure, could cause indirect momentary fluctuations in (dis)inhibition and whether these fluctuations were related to alcohol consumption. I hypothesised, based on previous research (Gauggel et al. 2010; Muraven and Shmueli 2006), that cue exposure would reduce inhibitory control and increase alcohol-seeking (Muraven and Shmueli 2006). Conversely, this was not the case in Chapter Six. Whilst alcohol cue exposure caused increases in alcohol-seeking (compared to water cue exposure) the mechanism driving this effect was not a transient decrease in inhibitory control. It is possible that the methodological limitation of not taking a baseline measure of inhibitory control may have contributed to this null result. However, as noted in Chapter 6.5, I decided that not taking this measure would counteract the effects of repeated cognitive tasks causing increases in disinhibition (Hagger et al. 2010; Huizenga et al. 2012). The results of this experiment do not support those from other chapters (Three and Five), which suggest more direct manipulations of inhibition can influence alcohol-seeking.

During the preparation of this thesis evidence had begun to emerge to suggest that drug cues may cause disinhibition in dependent and non-dependent samples, yet it was not demonstrated in Chapter Six. I suggested a possible reason for this is that in previous studies (Noël et al. 2007; Petit et al. 2012; Weafer and Fillmore 2012a) alcohol cues have been embedded directly into response inhibition tasks (i.e. the cue signals an inhibitory response: similar to the modified stop-signal task in Chapter Five, Experiment one). These tasks support the line of research that suggests alcohol cues ‘grab’ attention in heavy drinkers (Field and Cox 2008; Field et al. 2009) and that there may be a reciprocal relationship may exist between attentional bias and disinhibition (Weafer and Fillmore 2012a). The standard stop-signal task was used here in accordance with an experiment that demonstrated fluctuations in disinhibition

in clinical samples (Gauggel et al. 2010). Hence, it is possible that I did not directly replicate this effect as I did not recruit alcohol detoxified individuals, who due to a long drinking history are more sensitive to alcohol related cues (Gauggel et al. 2010; Noel et al. 2007). Furthermore, the explanation for the transient increases in disinhibition, according to Gauggel and colleagues, was a reduction in self-control (ego-depletion), as detoxified alcoholics that sniffed beer had to inhibit their impulses to drink (see also, Muraven and Shmueli 2006). It may be that in this case heavy drinkers did not have to actively restrain from drinking. Finally, Gauggel and colleagues' laboratory have recently failed to replicate their own findings of cue induced disinhibition (see Mainz et al. 2012) and this failure to replicate transient disinhibition in response to drug cues has emerged in other populations (i.e. opiate dependent patients; Verdejo-García et al. 2012), suggesting much more research is needed to clarify the possible mechanisms of cue induced disinhibition.

In partial support of de Wit's (2009) hypothesis that momentary fluctuations in disinhibition may lead to the (re)uptake in drug use, I did demonstrate that disinhibition was associated with subjective craving after cue-reactivity. This finding is theoretically important, as evidence suggests greater cue-reactivity is associated with relapse (Rohsenow et al. 1990). These results supported similar evidence by Papachristou and colleagues (2012b), who demonstrated that heavy drinkers with deficits in response inhibition showed greater cue-reactivity than light drinkers. Indeed, an increase in cue-reactivity may be moderated by alcohol availability (Papachristou et al. 2012a). Conversely, full support for de Wit's hypothesis is limited by the non-significant relationship between SSRT and *ad-libitum* alcohol-seeking in the alcohol cue exposure group.

8.1.2 Oculomotor disinhibition

Directly manipulating behavioural inhibition, both non specific and cue-specific, seems to have a causal role on alcohol-seeking. However, this thesis found no support for the causal role of oculomotor inhibition (Chapter Five, Experiment Two). Even though behavioural and oculomotor inhibition are assumed to represent

components of 'impulsivity' (Roberts et al. 2011; Weafer and Fillmore 2012a) and executive functioning (Bickel et al. 2012; Miyake and Friedman 2012; Miyake et al. 2000) the null results of the manipulation of oculomotor inhibition suggests that it does not have a causal influence on alcohol consumption. There are few possible reasons for these seemingly contradictory findings.

Firstly, whilst the evidence has demonstrated on a number of occasions the associations between behavioural inhibition and alcohol-seeking (Goudriaan et al. 2006; Verdejo-Garcia et al. 2008), there are relatively few studies which support the association between alcohol consumption and oculomotor disinhibition. The most pertinent study which has demonstrated a cross-sectional relationship was reported by Weafer et al (2011). In this study Weafer and colleagues compared the performance of individuals with ADHD to healthy controls on a delayed ocular return task and found ADHD individuals to be more disinhibited. Furthermore, the level of disinhibition within this subgroup was associated with greater reported consumption of alcohol. Consequently, it is unreasonable to draw inferences based on this as individuals with ADHD are more likely to suffer inhibitory control deficits, and the association was not present in healthy controls. However, we can draw influences from studies that have examined the effects of acute alcohol consumption on oculomotor inhibition. Specifically, Abrams et al (2006) demonstrated a dose dependent relationship between acute alcohol consumption and delayed ocular responses (a measure of oculomotor disinhibition). Similar results have also been reported comparing acute alcohol to placebo (Roche and King 2010). Secondly, a possible reason the manipulation did not affect alcohol consumption may have been due to the poor effects of the training on oculomotor behaviour. Compared with the non-specific and cue-specific effects of training motor inhibition, which were generally quite strong throughout, the effects of cue-specific oculomotor training on behaviour were comparatively weaker. There was only a significant increase in reaction times to pro-saccade trials on alcohol cues, again signalling anticipation to inhibit, but no effects on anti-saccade latencies or errors. Furthermore, in comparison with behavioural cue-specific training there were fewer actual training trials (80% compared to 90%), which may have contributed to the weakened effects. As such, any conclusions drawn upon the basis of this study must be provisional until replicated.

Therefore, it remains to be seen if oculomotor inhibition really does have a causal relationship with alcohol consumption. However, from the evidence available, I believe this is unlikely to be the case. Not only does acute alcohol reliably impair oculomotor inhibition (Abroms et al. 2006; Weafer and Fillmore 2012b) but chronic alcohol users also show impaired oculomotor performance (Campanella et al. 2009). Whilst the later does not provide conclusive evidence for causality it does suggest, in the absence of longitudinal evidence, that oculomotor disinhibition may be a consequence of alcohol induced neural toxicity. As I suggest in the discussion of Chapter Five, a possible explanation may be that manipulations of behavioural inhibition influence alcohol consumption because the act of drinking is a motor behaviour (similar to picking up a glass, walking into a bar), whereas the oculomotor inhibition (in this case the anti-saccade) task measures an innate reflex (Logan and Irwin 2000). We can assume that drinking behaviour does not represent an innate reflex, but rather a volitional behaviour reinforced over time.

8.1.3 Restraint beliefs

As well as investigate disinhibited behaviour, a second hypothesis of this thesis was to examine how beliefs about the ability to inhibit alcohol consumption (restraint beliefs about alcohol) also play a causal role in individuals' alcohol consumption. This experiment (Chapter Seven) was constructed in a similar way to previous experiments, with two specific hypotheses, i) that beliefs about restraint could be manipulated, and ii) the manipulation of these beliefs may influence individuals' alcohol consumption. This manipulation took the form of feedback following two tasks which participants were led to believe measured the ability to control their alcohol consumption. One of these tasks was a stop-signal task so that disinhibited behaviour could be measured. The findings from this experiment suggest that individuals who were led to believe they had high control (restraint) over their alcohol consumption, exhibited increased disinhibited behaviour (drank more alcohol) than those who were led to believe they had low control over their behaviour. Importantly, these effects transpired when actual levels of disinhibition were controlled for using a stop-signal task. This was the first experimental

evidence suggesting that beliefs about restraint can be manipulated within individuals and may play a causal role in alcohol consumption. The implications of these findings are discussed below (Chapter 8.4).

8.2 Individual differences in disinhibition and their association with *ad-libitum* alcohol consumption in the laboratory.

Throughout this thesis there was some evidence to suggest that individual differences in inhibitory control, particularly following direct experimental manipulations of (dis)inhibited mindsets, were associated with alcohol consumption. The association between disinhibition and drug use measures is rarely reported in the literature, especially measures of *ad-libitum* drinking. However, one example comes from Weafer and Fillmore (2008) who demonstrated that in intoxicated individuals the magnitude of disinhibition measured using a Go/No-go task was associated with *ad-libitum* consumption.

In the original disinhibition priming study (Jones et al., 2011a) I reported that individual differences in various indices of disinhibition were associated with alcohol-seeking but only in the group in which restraint was emphasized. In Chapter Three I partially replicated these results by demonstrating that throughout the whole sample, participants who responded with increased inhibition (slower reaction times and less inhibition errors on the stop-signal task) drank less alcohol during the taste-test. Similarly, an association between disinhibited behaviour and *ad-libitum* consumption was demonstrated in Chapter Four, however, this was only the case in the neutral / response conflict group. What I did find was intra-correlations between inhibition performance, a neuropsychophysiological component of inhibition and alcohol-seeking. This is a unique finding yet to be reported in the literature and not only provides evidence that the P300 neuropsychophysiological component is a marker of inhibitory control, but it is also associated with alcohol consumption.

In Chapter Seven there was no association with measures of inhibitory control and *ad-libitum* alcohol-seeking. However, this was not surprising considering the stop-signal task was modified by having large numbers of easy and difficult inhibition

trials, and restraint beliefs were the most important determinant of alcohol-seeking in this study. More so, in Chapter Six I found no significant association between SSRT and alcohol consumption in either group. This was surprising as it was hypothesised this would be the case. However, I did find that Stop-Signal Reaction Time was associated with measures of craving and urge when measured under cue exposure (discussed above). Whilst this did not directly support my hypothesis, it did support another emerging research area suggesting effective inhibitory control may be effective in reducing cue reactivity (Papachristou et al. 2012b). Finally, in the modified stop-signal and anti-saccade tasks there were no associations between inhibition and *ad-libitum* alcohol consumption. However, this may be due again to the tasks being modified.

The finding that measures of inhibitory control during the stop-signal task are associated with immediate *ad-libitum* alcohol consumption in social drinkers is relatively novel. It endured mainly when there were no methodological changes to the task (i.e. no added cues, and keeping the proportion of stop trials at 25%), but also when motivational bias was added to the task. Whilst a significant association was found within all three studies that used this method (Jones et al. (2011a), Chapter Three and Chapter Four), care must be taken in drawing firm conclusions from this finding as it was not consistently found in one specific experimental group. Nevertheless, there may be some merit in future studies in examining the associations between inhibitory control and *ad-libitum* alcohol consumption to increase our understanding of the relationship between the two.

8.3 Overall support of theoretical models of disinhibition in addiction

As discussed in Chapter One, the major theoretical models of addiction posit a relationship between disinhibition and alcohol use. In terms of impulsivity, the majority of evidence is cross sectional with measures of disinhibition being used to distinguish between drinking subgroups. For example, heavy drinkers exhibit increased disinhibited behaviour than light drinkers and alcoholics exhibit higher levels of disinhibition than non-alcoholics.

As well as the associations providing evidence for impulsivity models of addiction that postulates a cross-sectional association between impulsivity, specifically response inhibition and drug / alcohol consumption, the relatively robust finding (from Chapters Three, Four and Five) that direct manipulations of (dis)inhibition can influence alcohol consumption, is a unique contribution to the research examining alcohol and disinhibition. These findings are the first to support the hypothesis by de Wit (2009) which predicted that, i) disinhibition could fluctuate within individuals, and ii) these fluctuations may promote the (re)uptake of drug and alcohol use. Specifically, this is the first body of evidence to examine these claims in sober participants.

As well as supporting theoretical models, this research also provides an experimental parallel for developmental models of addiction (Nigg et al. 2006; Tarter et al. 2003; Wong et al. 2006). These models posit that the development of inhibitory control throughout adolescence is an important determinant of future alcohol consumption and possible risks associated and thus suggest that the rate in which inhibitory control develops influences alcohol consumption. The longitudinal studies described previously (Chapter 1.7) suggest that deficient response inhibition independently contributes to an increased risk for development of substance use disorders. Furthermore, the evidence suggesting a faster development of response inhibition provides resiliency against substance use disorders is particularly supported by the experimental studies here, which suggest exhibiting restraint, leads to a reduction in alcohol-seeking.

As well as supporting developmental evidence, the results from Chapters Three and Four also partially support recent claims that practicing self-restraint may inoculate individuals from engaging in health risk behaviours. For example, my findings directly support recent evidence from Muraven (2010) who demonstrated that practicing small acts of self-control, such as resisting sweets and squeezing a handgrip, can lead to an improvement in unrelated self-control performance, in this case abstaining from smoking. Furthermore, this improvement was protective against smoking relapse. Effective inhibitory control, and behavioural resiliency, was also shown to increase resiliency in the developmental models of addiction (Wong et al. 2006) and decrease the risk of alcohol ab(use). It may be that improving the ability to

inhibit behaviour (by placing an emphasis on restraint) has the same mechanisms of effect (albeit at only one point in time).

The non-specific and cue-specific inhibitory control increases also support the extensions to the dual process models of addiction. Specifically Friese et al's (2011) hypotheses that interventions based on i) improving the ability to self-control, or ii) changing reflective structures may both be beneficial in reducing health risk behaviours. Whilst evidence has begun to suggest changing automatic structures (i.e. attentional bias modification (Field and Eastwood 2005; Schoenmakers et al. 2010) and automatic associations (Wiers et al. 2011)) may reduce health risk behaviours the evidence presented in this thesis, as well as emerging evidence from Verbruggen et al (2012), suggest that situational improvements in inhibition can also protect against heavy drinking and other risky behaviours.

The evidence suggesting that alcohol induced neurotoxicity may be a cause disinhibition should also be considered here. The experimental manipulations described in this thesis demonstrate fluctuations in disinhibition can cause alcohol-seeking, demonstrating causality. However, this does not rule out the possibility that chronic alcohol use may also cause disinhibition through the mechanisms described previously (Chapter 1.6). Consideration of all the theoretical models (described in Chapter One), collectively suggests the most plausible hypothetic explanation is that pre-existing inhibition deficits (through developmental problems or impulse disorders) may pre-dispose individuals to substance (ab)use. Furthermore, the research presented in this thesis has shown that temporary disinhibited states can increase alcohol consumption at that particular moment in time. Over prolonged periods this ab(use) may cause neurotoxicity, leaving individuals at greater risk for further (ab)use (due to a reduced biological ability to exert inhibitory control), thus creating a positive feedback loop. I propose that non-specific and cue-specific restraint may be protective against temporary disinhibited states (through the mechanisms described above and in relevant chapters). It may also be possible to use these paradigms to reduce alcohol-induced disinhibition. Nevertheless, future research is needed to clarify these theories.

8.4 Overall support for relevant models of restraint beliefs in addiction

The demonstration that beliefs about restraint can play a causal role is a unique contribution to our understanding of possible processes underlying addiction. The relevant theoretical models of addiction discussed (in Chapter 1.12) hold opposing views for the role of restraint beliefs. In clinical models (Self-efficacy theory) it is widely accepted that beliefs in the ability to restrain from alcohol consumption (the opposite of disinhibited behaviour) is protective against relapse (Rollnick and Heather 1982) and as such, treatment models support this by aiming to increase confidence and targeting motivation to abstain (Marlatt et al. 1993). However, the experimental evidence for the Self-efficacy is relatively weak, particularly in alcohol consumption and non clinical samples (Gwaltney et al. 2009; Maisto et al. 2000).

In non-clinical samples, Nordgren et al (2009) argued a different effect of restraint beliefs - In that increased confidence in one's ability to control behaviour (restraint beliefs) will lead to increased disinhibited behaviour, and increased substance use. The specific hypothesis from this model that 'inflated self-control beliefs lead to increased disinhibited behaviour' was tested in Chapter Seven. It was pertinent to examine whether some experimental support for self-efficacy in non-clinical samples could be provided or if Nordgren and colleagues' predictions would be supported in heavy drinkers, as this would suggest that disinhibited behaviour as well as beliefs about inhibition may have paradoxical roles in alcohol consumption.

The results discussed in Chapter Seven generally support Nordgren and colleagues 'restraint bias' hypothesis. Specifically, if individuals were led to believe they had good restraint they drank more alcohol than individuals who believed they had less restraint. When we consider this alongside existing behavioural research (as well as the results presented in this thesis), that suggests exercising inhibitory control may be protective against substance (ab)use, they seem at first glance paradoxical. However, there is emerging evidence to suggest a point where belief in one's ability to restrain becomes overconfidence (Staring and Breteler 2004). This overconfidence may lead individuals to expose themselves to greater temptation or exhibit disinhibited behaviour. These findings are unique and if generalised to clinical samples may help inform treatment methods.

8.5 Comparisons between ‘state’ and ‘trait’ disinhibition

As discussed throughout Chapter One, the majority of theoretical addiction models examine or consider disinhibition to be a ‘trait’, relatively stable over long periods of time. Whereas both de Wit (2009) and I postulate here that disinhibition may also fluctuate and these fluctuations could be considered as ‘states’. The results described in this thesis do not serve to contradict the findings from models based on trait assumptions but rather support them. Evidence from ‘trait’ models consistently demonstrates behavioural disinhibition is associated with increased alcohol use, (Verdejo-Garcia et al. 2008). What was consistently found was that ‘state’ fluctuations in disinhibition have similar effects - albeit the majority of the results in this thesis were focused on improvements in inhibition being associated with decreased alcohol consumption, they still support the assumptions and evidence from these trait models as we assume disinhibition to be a continuous variable.

Given that research into personality constructs suggest the magnitude of a ‘trait’ is likely to determine the possibility of ‘state’ fluctuations (cf. the personality constructs of ‘ego control and ego resiliency’; which suggests individuals have a general level of control which can deviate somewhat in response to their circumstances (Carver 2005)), I can speculate that disinhibition may also operate in a similar way. Therefore, the similarities in the evidence for both ‘state’ and ‘trait’ disinhibition were not unexpected given the relatively homogeneous samples here. However, it remains to be seen for how long and how much these state fluctuations in disinhibition can deviate from individuals’ more general levels of inhibitory control (discussed briefly in terms treatment applicability below).

Limitations

8.6.1 Generalisation to those motivated to reduce drinking

Whilst the studies in this thesis had some success in establishing causality of disinhibition in alcohol-seeking they are not without limitations. In terms of their impact for future research, perhaps the most apparent limitation is the sample

population used here. Whilst important to establish causality in those at high risk for developing symptoms of alcohol abuse and dependence, dual process models suggest student and adolescent drinkers have little motivation to reduce their alcohol-seeking. Research suggests that students who drink heavily do so because it is considered a normative behaviour (Faulkner et al. 2006). For example, students and young adults begin to drink heavily due to a combination of increased risk taking (discussed in Chapter One) and because their social environment (i.e. University, or leaving the parental home) allows such behaviours (Littlefield et al. 2009). If there is no motivation to limit drinking then any possible clinical applications of these results, particularly cue-specific training and targeting restraint beliefs may prove futile.

Upon leaving university and reaching later adulthood many students become motivated to reduce their drinking. This is often referred to as ‘maturing out’ of alcohol use. The main reasons driving this motivation include health risks, work and family commitments (Littlefield et al. 2009). Therefore, it remains to be seen whether any possible interventions derived from this research (see Chapter 8.3 and 8.4) would translate to a reduction in health risk behaviours, specifically in individuals motivated to reduce their consumption. What was done in this thesis was to examine motivation using a self-report questionnaire (the Temptation and Restraint Inventory) and the main use of this was to control for possible group differences in this measure. However, this is an important point that needs to be addressed, as the dual process model of adolescent substance use implies motivation as a factor that influences alcohol consumption. The current studies are likely to be underpowered to examine moderating effects of self-reported drinking restraint on the experimental manipulations.

8.6.2 Task properties

A second possible limitation is inability to calculate SSRT in the direct manipulation studies. As discussed in Chapter One, the stop-signal task is a measure of action cancellation. That is, a pre-dominant response has likely been initiated before

stopping occurs. SSRT, which is the measurement of the response time from stop-signal onset to actual inhibition (which is unobservable), is unreliable as a measure of inhibition if there is a specific motivational bias in responding. This is due to assumptions required to calculate SSRT. For example, Logan and Cowen (1984) and Band et al (2003) argue that for SSRT to be robust subjects must not adapt strategies on the task, i.e. wait for the stop-signal tone. The standard stop-signal instructions emphasise speed on go trials and accuracy on stop trials as equally important. However, in the case of the Chapters Three and Four response strategies were necessary to prime disinhibited and restrained mindsets. Indeed, Leotti and Wager (2010) assessed the effects of such strategic responding on SSRT and concluded that reducing the speed accuracy trade off using subtle methods influenced SSRT as a measure of inhibition.

Finally, the stop-signal and modified stop-signal tasks in this thesis adapted the fixed delay paradigm. This is likely the most appropriate version of the task for the manipulation studies as the dynamic methods are designed in such a way that there will be close to 50% proportion of inhibition failures. This would be undesirable, particularly in Chapters Three and Four when priming individuals to restrain. If they repeatedly failed at their restraint, due to increasingly delayed stop-signal times, it is unlikely a potent mindset would be primed. I decided to keep the fixed delay version for the study examining indirect fluctuations of inhibition (Chapter Six) for consistency. However, it may not be the most effective method in these studies as the most popular method of calculating SSRT using fixed delays (the integration method) is most sensitive to violations of the horse race model.

I believe that benefits of these variations in the stop-signal task outweigh the potential limitations of using the Go/No-go task. As discussed (in Chapter 1.4.2) action cancellation is considered to be a more sensitive and powerful measure of disinhibition than action restraint. Furthermore, on the Go/No-go task individuals' performance is often close to ceiling with very little errors (Barch et al. 2009). Finally, as mentioned in Chapter Five, the stop-signal task is best suited to examine cue-specific training as the inhibition response is not made on initial stimulus presentation, unlike the Go/No-go task.

8.7 Future research

The findings of this thesis could not only inform theoretical models of addiction but also treatment methods. Future research should continue by providing further support to both. Specifically, there is now considerably more evidence supporting the premise that disinhibition may fluctuate both between individuals of a similar group (heavy drinkers), but also within these individuals. This was shown in a number of experiments in this thesis, using different methods such as influencing participants motivational bias to respond (see Chapters Three and Four), but also by increasing the frequency of inhibition to specific cues (see Chapter Five, Experiment one). Whilst important, both of these methods I refer to are more direct manipulations of inhibition. When I attempted to manipulate inhibition indirectly, by exposing participants to alcohol / neutral cues, no fluctuations were evident. This suggests that the transiency of inhibition is still not well understood, neither is the durability of these effects. Therefore, future research should begin to concentrate on understanding the causal and temporal aspects of indirect fluctuations.

Furthermore, it has recently been shown that cue induced fluctuations in inhibition may occur in response to non drug-specific cues i.e. in response to painful (Yu et al. 2012) or biological threat-like stimuli (i.e. spiders; Hartikainen et al. 2012). This presents the intriguing hypothesis that it may be generally arousing stimuli that cause disinhibition, rather than specific drug-related cues. This provides support to a recent hypothesis which suggest arousing stimuli compete for both attention and behavioural control mechanisms (Hartikainen et al. 2007). An interesting avenue for future research that could enhance our knowledge of disinhibition as a 'state' would be to examine if cue-induced fluctuations in disinhibition are specific or general. That is, whether drug-related cues influence disinhibition to a greater magnitude than general arousal-related cues in specific drug using sub-groups (heavy drinkers or alcoholics). This may provide support for models of addiction that posit drug users show increased arousal to their drug of choice but also would be beneficial when considering cue-specific inhibition training as a potential treatment adjunct (discussed below).

It is also important for future research to demonstrate the generalizability of cue-specific inhibition training, i.e. does training inhibition to specific alcohol cues cause increases in response inhibition to alcohol cues not used in the task or increases in response inhibition on other tasks. A similar line of research has been investigating these issues on the efficacy of attentional bias retraining and found low generalizability (Field et al. 2007). If cue-specific inhibition training has low generalizability then it may be a possible reason why I was unable to demonstrate reductions in drinking outside the laboratory.

Perhaps the most ambitious but also most informative direction for future research would be a longitudinal study that examined the interactive effects of both beliefs about restraint and state fluctuations in disinhibition on alcohol-seeking over a defined period of time, similarly to the ecological momentary assessment studies by Muraven et al (2005a, b). This would not only provide much needed longitudinal evidence about fluctuations in disinhibition but may also highlight when individuals are most at risk of loss of control and / or overconfidence.

8.8 Clinical applications of these findings

In terms of translating the findings of this thesis into targeting reductions in alcohol-seeking, both non-specific and cue-specific inhibition training may yield some positive results. Whilst the study presented in Chapter Five (Experiment one) showed cue-specific increases in inhibitory control decreasing alcohol consumption immediately, this did not translate to any follow-up measure. It could be that with repeated training to inhibit to alcohol cues these effects on alcohol consumption may persist outside the laboratory (if participants were motivated to reduce their consumption). If this was the case it would be comparable to attentional retraining research that suggests repeated training leads to clinically significant improvements outside of the laboratory (Schoenmakers et al. 2010), and would support the dual process hypothesis that strengthening both implicit and controlled processes can reduce health risk behaviours. One possible way to do this would be implementing the cue-specific inhibition tasks through the internet, or via a smart phone. This may

have the added benefit of training individuals to inhibit to cues in the environment which they are likely to be exposed to them (for example bars and pubs). Furthermore, if these sessions of repeated cue-specific inhibition training indeed serve to reduce alcohol-seeking then they may also reduce consumption of other drugs (such as nicotine, cocaine).

The findings from Chapter Seven suggest that a possible overconfidence in ones beliefs about restraint may have a paradoxical effect, (when compared with behaviour) on alcohol-seeking. Therefore, this evidence could also be used to inform treatment models. For example, whilst a degree of belief in one's ability to control their alcohol consumption is considered be beneficial, if these beliefs become unrealistic they may lead to increased exposure to 'high-risk' relapse situations such as entering a bar. Once in this bar they may not have the inhibitory control necessary to overcome urges to drink or state fluctuations caused by cues. Therefore, a combination of cue-specific inhibition training, as well as maintaining realistic beliefs about the ability to restrain may prove a clinically effective treatment combination.

8.9 Concluding Comments

In this thesis I examined the relationship between state disinhibition and alcohol consumption in heavy social drinkers. I focused on the specific hypothesis that (dis)inhibition may be a transient state that could be influenced by motivational bias, training and relevant cues and whether (dis)inhibition could influence alcohol consumption. I demonstrated that in response to motivational biases and cue-specific training (dis)inhibition could fluctuate within individuals, however, mere exposure to alcohol cues did not lead to increased disinhibition. These fluctuations influenced alcohol consumption which is some of the first experimental evidence of a causal effect of disinhibition in sober individuals. This effect transpired only for behavioural inhibition and not oculomotor inhibition, suggesting potentially different roles between the two in relation to substance use. Furthermore, I found that manipulating beliefs about inhibition had potentially paradoxical effects, highlighting the

distinctions between beliefs and behavioural effects of disinhibition on alcohol-seeking. Importantly, priming individuals with a motivational bias to inhibit and training individuals to inhibit behavioural responses specifically to alcohol cues, lead to a reduction in their alcohol-seeking. These results when examined together suggest that non-specific and cue-specific inhibition training may be a potential avenue for future treatment methods, as evidence is emerging to suggest that disinhibition is causally related to alcohol consumption.

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