IMPAIRMENT OF RESPONSE INHIBITION AND FLEXIBILITY: EFFECTS OF ALCOHOL AND INFORMATION PROCESSING

by

Craig Millar Easdon

A thesis
presented to the University of Waterloo
in fulfilment of the
thesis requirement for the degree of
Doctor of Philosophy
in
Psychology

Waterloo, Ontario, Canada, 1998

The University of Waterloo requires the signatures of all persons using or photocopying this thesis. Please sign below, and give address and date.

ABSTRACT

This thesis developed go-stop and change tasks to measure the effects of a moderate dose of alcohol on tasks of executive cognitive processes when low or high information processing was required to respond to go-signals. Two experiments, consisting of sixteen male social drinkers each, tested the performance of one group under .62g/kg alcohol (n=8) or under a placebo (n=8). Alcohol Study 1 demonstrated that alcohol impaired inhibitory control on a go-stop task, and the degree of impairment did not differ when the cognitive processing required to respond to a go-signal was increased. Alcohol Study 2 used a change paradigm task that replicated the findings of Alcohol Study 1 and demonstrated that alcohol impaired response flexibility by slowing the time required to make a second response following a failure to inhibit a first response. The results of the studies showed that alcohol can impair response inhibition and flexibility without affecting the reaction time to go-signals. Contrary to theories that propose alcohol impairment increases when information processing demands are greater, greater impairment under alcohol was not observed when the processing demands of the tasks were increased. Previous studies have typically used indirect, proxy measures of inhibitory control and response flexibility. In contrast, the present research built upon methods developed in cognitive science that directly measure response inhibition and flexibility. This approach made it possible to assess the effects of a moderate dose of alcohol on inhibitory control and response flexibility when the processing demands of the task were manipulated. The research has developed a novel approach for investigations of drug-effects on cognitive control of behaviour, and provides new information on the impairing effect of alcohol on cognitive processes.

ACKNOWLEDGEMENTS

I would like to thank Dr. Muriel Vogel-Sprott for her many contributions to the work presented in this thesis. Her clarity of mind and insightful comments helped to make this thesis stronger. I would also like to thank Dr. Vogel-Sprott for the invaluable guidance and support that she provided throughout my graduate training.

I am grateful and wish to extend thanks to committee members, Dr. Mike Dixon, Dr. Colin Ellard, Dr. Eric Roy, and Dr. Jim Frank, who offered constructive comments that helped to clarify the work presented in this thesis. And who would have thought it: a doctoral defence is like a box of chocolates...

Thanks to Joan and Garn Davey for helping me make it through grad school. The time spent in the your warm company provided welcome relief from a sometimes gruelling process.

Special thanks to my family, Betty, Les, and Laura, for continuing to support my endeavours and for expressing pride in my accomplishments. Your faith in my abilities has been constant and unyielding, and has sustained me over the years.

This research was supported by grant A8321 from the Natural Sciences and Engineering Research Council of Canada (NSERC).

DEDICATION

To Bella.

Too many thanks would be too few. I look forward to many more magical moondances together. Love always.

TABLE OF CONTENTS

TABLE OF CONTENTS (continued)

TABLE OF CONTENTS (continued)

TABLE OF CONTENTS (continued)

TABLE OF CONTENTS (continued)

Page

LIST OF TABLES

Page

LIST OF TABLES (continued)

Page

LIST OF FIGURES

Page

INTRODUCTION

Alcohol is the most widely used psychoactive drug in many societies. Commensurate with its wide usage, alcohol consumption plays an important role in many cultural events and religious ceremonies (McKim, 1991). Most drinkers consume alcohol without harming themselves or others. However, the use of alcohol by some individuals is linked to numerous types of serious social and personal difficulties. Alcohol use has been linked to anti-social, aggressive, violent and criminal behaviour, as well as to accidents and fatal injuries (NIAAA, 1992). Efforts to account for such harmful behaviours under alcohol have prompted research on the drug by many disciplines. One commonly advanced explanation is that alcohol impairs cognitive control of behaviour, particularly the ability to inhibit a response. This thesis reviews the evidence concerning this hypothesis, and presents a series of studies designed to test the effects of alcohol on response inhibition and flexibility.

ALCOHOL

Neuropharmacology

The term "alcohol" refers to a class of chemicals. However, in this thesis, alcohol will be used to refer to ethanol, or ethyl alcohol, which is the substance that humans consume. Alcohol is classified as a sedative/hypnotic drug. Alcohol is a small molecule that distributes easily and evenly throughout body water and crosses the blood-brain barrier (McKim, 1991). Unlike most drugs, alcohol does not act at a specific receptor site. Instead, alcohol acts more generally. One way that alcohol affects the nervous system is by acting on neuronal membranes. Alcohol makes neuronal membranes more fluid, resulting in a disordering of the molecules of the membrane and altering numerous cellular functions (Hunt, 1993). By

fluidising the cell membrane, alcohol disrupts both voltage-gated and receptor-mediated ion channels, thereby affecting both the conduction and synaptic transmission of neurons.

Neuropharmacological investigations have accumulated considerable information on how alcohol might affect brain function. The effect of alcohol on calcium ion channels makes the movement of calcium into the neuron more difficult, thus upsetting neurotransmitter release (Leslie, Barr, Chandler, & Farrar, 1983). The presence of alcohol also affects neuronal functions by altering the interaction between neurotransmitters and their receptors. These effects have been observed with the inhibitory neurotransmitter gamma-amino butyric acid (GABA) and with the primary excitatory neurotransmitter of the nervous system, glutamate. These actions of alcohol might contribute, respectively, to the sedative and stimulant effects of the drug (Hunt, 1993). Research also indicates that, at low concentrations, alcohol interferes with the binding of N-methyl-D-aspartate (NMDA) to its receptor (Lovinger, White, & Weight, 1989). As NMDA is thought to be involved in learning and memory, the interference of alcohol with NMDA might contribute to the impairment of these functions under the drug. Research further indicates that the presence of alcohol is associated with a release of dopamine (DA) in both the nucleus accumbens (NA) (Imperato & Di Chiara, 1986) and the ventral tegmental area (VTA) (Gesa, Muntoni, Vargui, & Mereu, 1985) of the brain. These effects of alcohol might be implicated in both the rewarding and addictive properties of the drug (Wise & Bozarth, 1987).

Recent research investigating the effects of alcohol at the level of the neuron has provided new insights on how the drug might affect brain functions. However, it is difficult to generalise these results to the effects of alcohol on the inhibitory control of behaviour. The

finding that alcohol interferes with both the inhibitory neurotransmitter GABA and the excitatory neurotransmitter glutamate hints at the complexity of the drug's action on brain function. Furthermore, to date, none of the changes in neuronal functioning in the presence of alcohol have been found to produce a particular drug-induced change in the behaviour of intact functioning organisms (Hunt, 1993).

Behavioural effects of alcohol

Decades of research have investigated the effects of alcohol on a variety of cognitive, perceptual and motor skill tasks performed by social drinkers (i.e., individuals with no history of any alcohol-related problem). Periodic reviews of the findings typically conclude that moderate doses of alcohol that achieve peak blood alcohol concentrations (BACs) of 80 mg/dL can impair most types of tasks to some extent (e.g., Carpenter, 1962; Holloway, 1995). Some evidence suggesting that cognitive-type tasks are impaired at lower BACs than tasks requiring primarily motor responses has led to the speculation that cognitive activities are particularly sensitive to the effects of alcohol (Mitchell, 1985).

A number of investigators have suggested that alcohol's disruptive effect on cognitive performance might reflect a reduction in efficient information processing under the drug (e.g., Moskowitz, 1973). It has also been suggested that impaired information processing might account for some of the inappropriate, extreme or deviant, behaviours displayed by drinkers. However, there is little agreement on the particular cognitive process, or processes, that are affected by the drug. Pernanen (1976) proposed that alcohol impairs cognitive functioning by reducing the capacity to extract and process cues from the environment. Others have suggested that alcohol interferes with information processing by restricting the focus of

attention to immediate and central environmental cues at the expense of peripheral cues (Steele & Josephs, 1990). This latter hypothesis, termed "alcohol-induced myopia", was advanced on the basis of drinkers' self-reports of the effect of alcohol, and no direct evidence of the effect of alcohol on perceptual or attentional processes was provided. Although this theory has since been invoked as a post-hoc explanation for the effects of alcohol on behaviour, and attitudes toward risk-taking behaviour (e.g., MacDonald, Zanna, & Fong, 1995), the assumptions underlying the theory have not been tested. One reason for the lack of experimental research testing "alcohol-induced myopia" might be that operational definitions of central and peripheral cues are lacking. As peripheral cues can only be identified when they fail to affect a response under alcohol, any "myopia"-based explanation for behaviour becomes circular, and is by necessity post-hoc.

Although the particular cognitive processes affected by alcohol have not yet been identified, one widespread assumption about alcohol is that it impairs the ability to inhibit behaviour. This lack of inhibitory control has been invoked to account for inappropriate behaviours under alcohol. The notion that behavioural disinhibition is caused by alcohol use is also incorporated into dictionary definitions of intoxication: "to make drunk, to excite or elate beyond self-control" (Oxford English Dictionary, 1991), "a loss of inhibition or control" (Collins English Dictionary, 1979). Furthermore, the idea that alcohol reduces self-restraint appears to carry considerable currency among the drinking public. It is not uncommon for individuals to claim that the behaviour they displayed under alcohol would never have been displayed had they been sober.

Behavioural disinhibition

The link between alcohol use and disinhibited behaviours that are socially inappropriate has been investigated extensively. For example, based on a cross-cultural review of 9304 criminal cases, Murdoch and Pihl (1990) reported that 62% of people charged with violent offenses and 45% of their victims were legally intoxicated at the time of their crime. The effect of alcohol on inappropriate social behaviour has also received much attention in laboratory studies. Some experimenters have employed competitive game scenarios, wherein subjects have the choice to subtract points from a bogus opponent. The measure of anti-social behaviour in such paradigms is the number of points participants are willing to take from their opponent. In general, evidence from such studies has indicated that a moderate dose of alcohol increases the amount a player is willing to subtract from his opponent (Cherek, Steinberg, & Manno, 1985; Cherek et al., 1990). Other researchers have attempted to evaluate the effects of alcohol on aggression in the laboratory by giving a subject the opportunity to shock a bogus partner. Subjects are informed that they are participating in an experiment designed to study the effects of aversive stimuli (i.e., shock) on learning. The level and duration of shock administered to the partner is then used as the measure of aggression (Zeichner & Pihl, 1979, 1980). Studies employing the shock-paradigm have had mixed results, but it has been observed that intoxicated subjects give shocks of longer duration, but not necessarily of higher intensity than do either sober controls or placebo controls (e.g., Pihl et al., 1981). Other investigators have noted that consuming alcohol increases the likelihood of engaging in diverse inappropriate social behaviours, ranging from verbal abuse (Rohsenow & Bachorowski, 1984) to writing graffiti (Korytnyk & Perkins, 1983).

In an attempt to obtain an overview of the effects of alcohol on anti-social behaviour, a number of researchers have analysed the results of the various studies using meta-analytic procedures. For instance, Steele and Southwick (1985) reviewed 34 studies that examined the effects of alcohol on a variety of social behaviours, including public speaking, gambling, and aggression. Steele and Southwick (1985) argued that the consumption of alcohol in a high-conflict situation would result in more extreme behaviour. Conversely, when alcohol was administered in low-conflict situations, less extreme responses would be observed. The results of their meta-analysis led them to conclude that the pharmacological effects of alcohol interacted with situational variables to produce deviant behaviour. A more recent meta-analysis by Ito, Miller and Pollock (1996) focussed specifically on the effects of alcohol on aggression and included studies with a variety of dependent measures of aggression. This meta-analysis led to the conclusion that, in general, alcohol increased aggression in studies conducted under both high- and low-conflict conditions. However, the authors also reported that the size of the effect depended on the type of measure of aggression used.

Although there appears to be some consensus in the literature that alcohol facilitates extreme social behaviours (e.g., Bushman & Cooper, 1990), the study of these relations in the laboratory environment is associated with a number of difficulties. Ethical and moral constraints make it almost impossible to study behaviours such as "real world" aggression in the laboratory. In addition, as studies of the effects of alcohol on behaviour have used different operational definitions of extreme social behaviours, results from these studies are difficult to compare. A more basic criticism is that most researchers use an increase in response measures (e.g., more shocks administered) to infer disinhibiting effects of the drug.

Response inhibition itself is not measured directly. Researchers interpret the willingness to give a shock of longer duration under alcohol as a measure of aggression, which is in turn interpreted as evidence of compromised inhibitory control under the drug. Moreover, although researchers (e.g., Steele & Southwick, 1985) posit that a reduction in cognitive and perceptual processing is central to the effects of alcohol on inhibitory control, the specific mechanisms that are affected by alcohol are not measured or identified.

Although research investigating the effects of alcohol-induced disinhibition and social behaviour suffers from a number of problems that limit its interpretation. this work does appear to indicate that the adaptive control of behaviour is poorer under alcohol. It is noteworthy that a great deal of research in neuropsychology indicates that the frontal cortices might play a significant role in the executive management of such behaviour.

NEUROPSYCHOLOGY

Background

Neuropsychologists' interest in the role of the frontal cortices in coordinating complex behaviours can be traced to the now classic case of Phineas Gage in 1848. Following damage to his left orbitomedial frontal cortex, Gage's personality reportedly underwent a significant change and he exhibited behaviours consistent with "poor planning" and "uncontrolled impulsivity" (Fuster, 1997, p150). Although early studies of the role of frontal lobe function were plagued by methodological flaws, a comprehensive review of these studies by Feutchwanger (1923) reported that individuals with frontal lesions tended to be apathetic and demonstrated deficits in planning behaviour. Feutchwanger further noted that memory and general intellectual functioning did not appear to be adversely affected in these patients.

Additional evidence, derived from the large number of frontal lobe leucotomies carried out during the 1930s and 1940s, appeared to confirm these conclusions (Fuster, 1997).

Current research emphasizes the anatomical complexity of the interconnections between the frontal cortices and other cortical and subcortical regions (e.g., Pandya & Barnes, 1987). For instance, the frontal lobes send and receive information from the hypothalamus, the amygdala and hippocampus (Damasio & Anderson, 1993). Furthermore, connections between the frontal cortices and the limbic system might affect the control of emotion (Kolb & Whishaw, 1996). To identify the brain regions implicated in the management and control of behaviour, researchers have employed two main methods. The first methodology is structural. This approach identifies individuals with known lesions to the frontal cortices and observes their performance on tasks. The second approach uses functional neuroimaging techniques to identify brain regions that differ in their metabolic rate during task performance. Although a number of cortical and subcortical structures have been implicated in the formulation and implementation of adaptive behaviours, both structural and functional research methods have suggested the involvement of the frontal and prefrontal cortices (Brodmann's areas 8, 9, 10, 11, 46) (Robbins, 1996).

Frontal lobe damage has been associated with a variety of deficits (Fuster, 1997). However, individuals with damage to the frontal cortices typically display behavioural deficits that are characterised by impaired planning and sequencing, and by inflexibility and perseveration (Kolb & Whishaw, 1996).

(i) Impaired planning and sequencing: Individuals with lesions to the frontal cortices show deficits in the planning and sequencing of behaviour on a number of

neuropsychological tasks. For instance, Shallice (1982) noted that individuals with frontal lesions performed poorly on the "Tower of London" task. This task requires the ability to outline a series of moves in order to complete a puzzle in the fewest number of steps possible. Shallice observed that, compared to controls, patients with frontal lobe lesions made more errors of perseveration and were less able to generate alternate strategies on the task. Petrides and Milner (1982) further noted that frontal patients often break the rules when performing neuropsychological tasks, even though they can state the rules when asked. For example, on tasks of verbal fluency where subjects have to generate four-letter words beginning with a certain letter, frontal patients might produce shorter or longer words starting with different letters. However, when questioned, these individuals can explain the task instructions correctly.

Additional corroboration for the involvement of the frontal cortices in planning behaviour comes from functional brain-imaging studies in neurologically-intact individuals. Using positron emission tomography (PET) to measure glucose metabolism, Jonides et al. (1993) found that activity in the dorsolateral frontal cortices increased on tasks requiring individuals to mentally order a sequence of actions to achieve a goal. This evidence suggests the importance of the frontal cortices in planning and executing behavioural strategies.

(ii) Inflexibility and perseveration: Frontal patients characteristically display an inability to adjust their behaviour when presented with environmental cues indicating that a change in response is required. This deficit can manifest itself as response perseveration. Neuropsychological tests reveal that, relative to controls, patients with damage to the frontal cortices perform poorly on tasks requiring flexible changes in responding. For example, on

the Wisconsin Card Sorting Test (WCST) these patients make many perseverative errors and are often unable to alter their response set once it is established, despite negative feedback (Petrides & Milner, 1982).

Using PET to measure glucose metabolism in neurologically-intact individuals, Frith et al. (1991) noted that the dorso-lateral prefrontal cortex (DLPFC; Brodmann's area 46) had a higher metabolic rate when a change in response strategy was required on a word-choice task. Taken together, the evidence from functional imaging in normals and the neuropsychological performance of patients with frontal lobe damage suggests that intact frontal cortices might be important in determining the ability to alter strategies "on-line".

(iii) Neuropsychological theories of frontal lobe function: Luria (1980) suggested that the frontal cortex "synthesizes information about the state of the external objective and the internal subjective worlds". Performance deficits observed in individuals with frontal lobe lesions, and functional neuroimaging in individuals with intact frontal cortices, have indicated the involvement of these regions in planning and sequencing behaviours, as well as the ability to alter one's actions in response to environmental cues. Based on this evidence, a number of current theories of frontal lobe function have suggested that the frontal cortices are involved in executive control of behaviour. Although the details of these theories differ somewhat, a common theme is that the frontal cortices are important in the processing and evaluation of environmental information, and in the formulation and execution of adaptive plans of action (e.g., Damasio, Tranel, & Damasio, 1990; Ingvar, 1985, 1996; Shallice & Burgess, 1991, 1993). Thus, damage to the functioning of the frontal cortices might disrupt the cognitive control of behaviour, thereby resulting in maladaptive behaviours.

Acute Alcohol Intoxication

A number of researchers have noted that the performance of subjects under a moderate dose of alcohol resembles that observed in individuals with mild damage to the frontal cortices (e.g., Adams et al., 1990; Pihl & Peterson, 1991). However, an extensive electronic literature search revealed few studies that have used clinical neuropsychological tests to assess the cognitive functioning of nonalcoholic individuals under a moderate dose of alcohol.

Zeichner and Pihl (1979) noted that mildly intoxicated social drinkers showed deficits in planning and abstraction on neuropsychological tasks. To test this hypothesis, Peterson et al. (1990) evaluated the effects of a moderate dose (.66 ml/kg) and a high dose (1.32 ml/kg) of alcohol on performance on a battery of neuropsychological tasks. Results indicated that the groups who received the high dose of alcohol performed significantly more poorly on tests associated with frontal lobe function (Porteus Maze, Word Fluency, Rey-Ostereith Complex Figure Copy) and temporal lobe function (Logical Memory Delayed Recall, Rey-Ostereith Delayed Recall) than did either the moderate dose group or a placebo control group. Peterson et al. argued that these results demonstrated that an acute dose of alcohol disrupted cognitive skills measured by tests of frontal lobe function. This finding was interpreted as corroborating that of other researchers who noted that abstract reasoning, decision making, and concept formation are impaired in social drinkers at moderate-to-high levels of intoxication (Tarter et al., 1971; Jones, 1974; Bates, 1989). As a caveat to this interpretation, it is worth noting that the paucity of published research reporting impaired performance on clinical neuropsychological tasks under a dose of alcohol might be the result of null findings that have gone unreported. For instance, in a study using a moderate dose of alcohol, intermediate to

the doses used by Peterson et al. (1990) (.62 g/kg = .83 ml/kg), no alcohol-induced impairment was observed on a battery of neuropsychological tests of executive cognitive functioning (Trail Making Task, Porteus Maze Task, Word Fluency) (Easdon & Vogel-Sprott, 1996a). This result suggests that the sensitivity of these clinical instruments might be too low to measure changes in a moderately intoxicated, neurologically intact population.

Functional neuroimaging studies of the effects of an acute dose of alcohol on blood flow in non-alcoholic individuals have produced varied results, possibly owing to inconsistencies in the amount of ethanol administered. Studies that have measured the effects of alcohol on regional cerebral blood flow (rCBF) using single photon emission tomography (SPECT) indicate that a moderate dose of alcohol (0.6-0.8 g/kg) results in increased global rCBF, whereas higher doses (>1.0 g/kg) reduce rCBF. Schwartz et al. (1993) measured rCBF in 24 nonalcoholic males following the consumption of 0.6 g/kg absolute alcohol and found a significant increase (4%) in global cortical rCBF. Other researchers have noted that the effects of alcohol on rCBF are more localised. For example, Newlin et al. (1982) noted that the increase in rCBF was bilateral in the posterior regions, but was greater in the right anterior region than in the left anterior region. Volkow et al. (1988) observed that a moderate-to-high dose of alcohol (1g/kg 95% U.S.P) increased blood flow to the right temporal and prefrontal cortex. Few studies have examined the effects of an acute dose of alcohol on local cerebral rates of glucose metabolism (LCMRGlc). A PET study in healthy young males administered 0.8 g/kg alcohol and found a global decrease in glucose metabolism (de Wit et al., 1990). This decrease was found to be most pronounced in the frontal cortex and in the cerebellum.

In summary, there is some evidence that a moderate-to-high dose of alcohol can impair

the performance of social-drinkers on neuropsychological tasks that measure executive cognitive functioning, and can alter the metabolic functions of the frontal cortices in social drinkers. Thus, it could be argued that by disrupting the functioning of the frontal cortices, alcohol might impair cognitive processes controlling behaviour and these effects of the drug could account for many aspects of behavioural impairment displayed under alcohol. It has been noted that neuropsychological tasks used to identify deficits in executive cognitive functions require cognitive inhibitory processes (e.g., Lezak, 1983). Research in cognitive science also suggests that inhibitory processes play an important role in the cognitive control of behaviour (e.g., Arbuthnott, 1995). However, clinical neuropsychological tasks do not measure the ability to inhibit a response directly, and the possibility that alcohol impairs inhibitory control remains circumstantial.

COGNITIVE NEUROSCIENCE

Inhibitory control

Imagine the student who, late for a final exam, is running full-tilt across a busy intersection and must stop abruptly to avoid being hit by an oncoming vehicle. Now consider the case of a bar patron who is being rudely pushed in the back, and is prepared to retaliate when the bar's bouncer suddenly tells him to stop. The ability to halt an ongoing response is essential to adaptive behaviour.

Some cognitive scientists have proposed that inhibitory control is an executive cognitive process (Logan & Cowan, 1984; Logan, 1994). Their theory conceptualizes inhibitory control as a race between two independent processes: a "go" process and a "stop" process. According to the race model, when a stimulus for a response is presented, a "go-

process" will be initiated. If the "go-process" runs to completion, then the response will be observed. However, if a stimulus indicating that a response should be withheld is also presented, then a "stop-process" is initiated, and the go- and stop-process will "race" one another to completion. If the go-process finishes before the stop-process, then a response will be observed. However, if the stop-process finishes before the go-process, then the response will be inhibited.

To measure inhibitory control, the race model employs a go-stop paradigm (also referred to as "Go/NoGo" task, e.g., Fenwick et al., 1993; Malloy et al., 1993). A go-stop paradigm engages individuals in a task where they respond to some go-signal. On a set percentage of trials, the presentation of the go-stimulus is followed by a second stimulus (the stop-signal) that tells the participant to withhold his response to the go-signal. When the stop-signal is placed very close in time to the go-signal (e.g., 50 ms following the onset of the go-signal), it is generally quite easy to withhold the response and many inhibitions are observed. However, when the stop-signal is moved further in time from the go-signal (e.g., 450 ms following the onset of the go-signal), it becomes increasingly difficult to withhold a response, and fewer inhibitions are observed. Thus, a go-stop paradigm provides a direct measure of inhibitory control in terms of the number of times an individual withholds a response when a go-signal is followed by a stop-signal.

One implication of the assumption of independence between the go- and stop-process is that increasing the cognitive or perceptual processing demands necessary to complete a go-response should slow its completion, thus more inhibitory control should be observed. Logan (1994) predicted that when the go-response is completed more slowly, then more stop-

responses should be completed first, and this should result in more inhibitions. A study by Riegler (1986) tested this prediction indirectly by varying the number of key presses required to complete a go-response, and found that this assumption of the race-model was tenable.

The go-stop paradigm can be made more complicated by requiring a different overt response to the stop-signal. This variation on the go-stop paradigm is referred to as the "change" paradigm (Logan & Burkell, 1986). It is of interest because, in addition to requiring subjects to respond to go-signals and withhold responses to stop-signals, subjects must also make some other overt response to the stop-signal. The inhibition of one response and the display of another is of interest because the ability to reengage -or switch- a response following a stop-signal is thought to indicate response flexibility. Thus, the change-paradigm allows for the direct investigation of both inhibitory control and response flexibility within a single task (Logan, 1994).

Go-stop paradigms have been used to explore stopping ability across a variety of activities, including type-writing, button pressing, speech production, and arm-swinging (Logan & Cowan, 1984). These paradigms have also been used to investigate behavioural deficits in populations known to demonstrate impairments of inhibitory control. Of particular relevance to the discussion of the involvement of the frontal cortices in deficits of inhibitory control is the finding that individuals with damage to the orbitomedial (OM) frontal cortex show deficits of inhibitory control on go-stop tasks (Malloy, Bihrle, Duffy, & Cimino, 1993). Studies using topographic evoked potential mapping in neurologically-intact normals also have found increased activity in the OM frontal areas during go-stop tasks (Kok, 1986; Malloy, Rasmussen, Braden, & Haier, 1989). Go-stop paradigms have also been used to

investigate the executive cognitive functioning of children diagnosed with attention deficit hyperactivity disorder (ADHD). Schachar et al. (1993) report that, relative to age-matched controls, children with pervasive ADHD demonstrate impairments of inhibitory control on the go-stop paradigm. Of further interest, it has been reported that a moderate dose of methylphenidate improves the performance of ADHD children on the go-stop paradigm (Tannock, Schachar, & Logan, 1995). Research using a change-paradigm has replicated the finding that children with pervasive ADHD show impaired inhibitory control relative to age-matched controls. This research also indicated that pervasive ADHD impairs the ability to reengage a second response (Schachar, Tannock, Marriot, & Logan, 1995). These results have been interpreted as indicating that pervasive ADHD affects both the inhibitory control and response reengagement components of cognitive flexibility.

Summary Overview

Evidence from cognitive science shows that a go-stop paradigm provides a direct measure of inhibitory control, and also demonstrates that response flexibility can be measured directly by a change paradigm. It appears that the use of these paradigms to study inhibitory control and response flexibility under alcohol could circumvent the problems inherent in proxy measures of these phenomena. These paradigms have additional procedural and theoretical advantages that make them well-suited for investigating the effects of alcohol on behaviour. The go-stop and change paradigms utilize computerised tasks that the subject performs alone in the laboratory. This procedure excludes many of the actual or perceived consequences that have clouded the interpretation of other studies that have investigated the disinhibiting effect of alcohol on social behaviour. To date, most research on alcohol-induced

behavioural disinhibition has aimed to determine whether or not it occurs. However, the extensive research and theory of inhibitory control based on the go-stop paradigm offers a guiding framework for investigating and predicting alcohol effects on behavioural inhibition.

To date, it appears that only two studies have investigated the effects of a moderate dose of alcohol on inhibitory control using go-stop tasks. Mulvihill, Skilling, and Vogel-Sprott (1997) investigated the effects of a moderate dose (.62 g/kg in males) of alcohol on inhibitory control using a go-stop task that placed stop-signals at fixed delays following the onset of the go-signal. In this task, the go-signal consisted of one-of-four letters (A,B,C, or D) presented on a computer monitor and subjects were instructed to press one key when they saw A or C and a second key when they saw B or D. On approximately 25% of trials, the go-signal was followed by a stop-signal (a 900 Hz tone) at either 50, 150, 250, or 350 ms following the onset of the go-signal. Findings from this study indicated that fewer total inhibitions were made under alcohol relative to drug-free performance and that reaction time to the go-signal was not affected by alcohol. Another experiment used a go-stop task in which subjects had to make a speeded choice between two targets (X or O) presented one at a time on a computer screen (Easdon & Vogel-Sprott, 1996c). In this study, a subject's performance was monitored trial-by-trial and the temporal presentation of the stop-signal was varied to estimate the time at which the stop-signal had to be delayed so that each subject would inhibit his response to a stop-signal 50% of the time. In accord with the results of Mulvihill et al. (1997), this study also showed that a moderate dose of alcohol (.62 g/kg) did not affect the reaction time to go-signal, but that stop-signals had to be placed closer in time to the go-signal for subjects to inhibit 50% of the time.

RATIONALE AND HYPOTHESES.

The evidence that a moderate dose of alcohol can impair inhibitory control without affecting response time to the go-signal is consistent with the race-model assumption that go- and stop-processes are independent. Thus it appears that the race model might be useful in predicting the effect of alcohol on inhibitory control when some parameters of the go-stop task are changed.

A theme in studies investigating the effects of alcohol on inhibitory control is that alcohol exerts its effect by disrupting information processing. The go-stop and change paradigms allow for the manipulation of the information processing demands of these tasks, and provide predictions about the effect of these manipulations. One prediction is that increasing the information processing demands required to process and execute a response to the go-signal will slow its completion, thus affording more time for the completion of the inhibitory process. Applying this logic to the study of inhibitory control under alcohol results in the prediction that inhibitory control should be better when the cognitive demands of completing a go-response are increased. This prediction is particularly interesting because it seems counterintuitive. The notion that alcohol impairs information processing would suggest that as the cognitive demands of a task are increased, greater impairment of inhibitory control should be observed.

The effect on inhibitory control of manipulating the information processing demands of the go-signal under alcohol is also of theoretical interest because it tests the race model assumption of independent go- and stop-processes. Research has shown that a moderate dose (.62 g/kg) of alcohol does not affect response reaction time to go-signals. Thus, the degree of

impairment in inhibitory control should not change when the cognitive demands for the initiation of the go-response are increased. On the other hand, if alcohol affects information processing, then go-stop task performance should be affected by increasing the demands of the go-signal. The response time to the go-signal might be slowed, or it might be maintained at the expense of inhibitory control. The first study in this thesis employed a go-stop paradigm to test the effect of a moderate dose of alcohol (.62 mg/kg) on inhibitory control when the information processing demands of the go-signal were manipulated.

The second study in this thesis extended the investigation to the effects of a moderate dose of alcohol on inhibitory control and behavioural flexibility using a change paradigm. This question is important because cognitive flexibility is thought to consist of both the ability to interrupt an on-going response and the ability to reengage responding on a secondary task. Evidence from neuropsychological testing suggests that a moderate dose of alcohol should disrupt the ability to switch efficiently from one task to another. The change paradigm affords a more direct evaluation of the ability to switch from one response to another than do clinical neuropsychological instruments (e.g., WCST) which must infer this deficit. Thus the main hypothesis tested in the second study was that, if a moderate dose of alcohol impairs response flexibility, then the ability to inhibit one response and to switch efficiently to another should be reduced under alcohol.

ALCOHOL STUDY 1

Study 1 used a go-stop paradigm to test the effect of alcohol on inhibitory control when the information processing demands required to complete a go-response on a go-stop task were increased. No research has been designed to examine the possibility that the effects of alcohol on response inhibition might interact with the cognitive demands of a task. This question is important because a central theme in explanations for the disruption of behavioural control displayed under alcohol is that alcohol impairs the ability to extract and process cues from the environment.

In order to conduct the present research, it was first necessary to develop two go-stop tasks that differed only in the amount of processing required to complete a go-response. Details outlining the rationale and development of these tasks, and their application to drug-free performance, are presented in Appendix A. That work resulted in the successful development of a "low-load" go-stop task (LGS) and a "high-load" go-stop task (HGS). To respond to the go-signal on the LGS, subjects were required to distinguish between two target letters presented one at a time on a computer monitor. To respond to a go-signal on the HGS, subjects had to distinguish between the same two target letters presented among a string of distracter letters. On both tasks, stop-signals occurred on approximately 27% of the trials. In accord with the race-model of inhibitory control, the results of drug-free performance indicated that response reaction time to the go-signal (RTGO) was significantly slower on the HGS task (410ms, SD=44) than on the LGS task (350ms, SD=40), and more inhibitions were made on the HGS task (52%) than on the LGS task (39%). The response accuracy to the go-signal on the tasks did not differ significantly (95% and 93%, respectively).

This study tested the following hypotheses:

(1) if a moderate dose of alcohol impairs inhibitory control on go-stop tasks, then alcohol should reduce the number of inhibitions made on both the LGS and HGS tasks as compared to a placebo.

(2) if a moderate dose of alcohol does not affect the response to the go-signal, then the response time to the go-signals under alcohol and placebo should not differ on either the LGS or the HGS task.

(3) if alcohol disrupts the ability to process more demanding information from the environment, then two different predictions are possible: either (a) inhibitory control should be more impaired under a moderate dose of alcohol on the high-load task than on the low-load task, whereas RTGO on the tasks should not be affected, or (b) alcohol should slow the RTGO for the high-load task, whereas the degree of impairment in inhibitory control on the low- and high-load tasks should not differ.

Method

Subjects

Sixteen right-handed males, age 19-22, were recruited from the University of Waterloo Cognitive Subject Pool. Subjects were healthy social-drinkers and were not taking either prescription or over-the-counter medication at the time of the study. Subjects agreed to fast for 3.5 hours prior to the treatment session, and received $15.00 for their participation in the study. Ethical approval for this research project was obtained from the University of Waterloo Office of Human Research.

Apparatus

Tasks. The performance was measured on two go-stop tasks. These tasks were programmed using Micro Experimental Laboratory (MEL), version 2.0, software (Pittsburgh, PA., 1995). Tasks were run using a 386/33 PC.

(1) Low-load go-stop task (LGS): This go-stop task required the subject to discriminate between an "X" and "O", presented one at a time on a computer screen, by pressing one of two keys on a keyboard. Each subject was seated 60 cm from the computer screen. The presentation of each letter was preceded by a prepatory fixation point (.) for 500 ms. Each letter was 1 cm in height and .5 cm in width and was presented at the centre of the computer screen for 500 ms. Subjects rested the index and middle finger of their right hand on two adjacent keys on the computer keyboard and responded to the stimulus by pressing one of the two keys. If "X" appeared, then the right key was pressed; if "O" appeared, then the left key was pressed. Subjects were instructed to respond as quickly and as accurately as possible. They were also told to try to withhold their response whenever a go-signal was followed by a stop-signal. The stop-signal was a 900 Hz tone presented for 500 ms following the onset of the go-signal. Stop-signals were presented infrequently (on approximately 27% of trials) and in a pseudo-random order, with no more than three stop-signals occurring in succession. Based on prior testing (see Appendix A), an equal number of stop-signals was presented at 60, 135, 210, and 285 ms following the onset of the go-signal.

Each letter presentation constituted one trial, and trials were separated by 1.5 seconds. One test consisted of 176 trials. Each test was presented in two blocks of 88 trials, separated by a 30 second rest period. Each block of 88 trials included 24 stop-signals, with 6 stop-signals at each of the four delay intervals. A block took 3 minutes and 45 seconds to complete

and a test took 7 minutes and 45 seconds to complete.

(2) High-load go-stop task (HGS): This task was identical to the LGS task, except that the go-signal target letters ("X" and "O") were presented along with five distracter letters (R, S, T, B, N) in a horizontal string in the centre of the computer screen. The order of the letters in each string was varied pseudo-randomly. Each of the target letters ("X" and "O") appeared 15 times in the first, second, third, and fourth positions, and 14 times in each of the fifth and sixth positions of the letter strings in each test. One target letter was present on each trial, and 88 trials were presented in two blocks for a total of 176 trials per test. Within each test, stop-signals were evenly distributed across each target letter and each string position; that is, each stop-signal delay occurred once for each of the target letters at each of the string locations (i.e., 4 delays x 2 targets x 6 locations = 48 stop-signals). All other aspects of this task were identical to the LGS task.

The number of inhibitions at each stop-signal delay and the total number of inhibitions displayed by a subject were recorded on each test, as well as reaction time to the go-signal when no stop-signal was present (RTGO). Although no hypotheses concerning response accuracy were made, the percentage of trials on which the subject pressed the correct key in response to a go-stimulus when no stop-signal was present was also recorded during the tests. The same measures of performance were obtained on each task.

Each subject performed the task alone in a room. The presentation of stimulus trials in two blocks during a test were controlled by the computer.

Blood alcohol concentrations (BACs). BACs were measured from breath samples using a Stephenson Model 900A Breathalyser.

Drinking habits. Subjects filled out the Personal Drinking History Questionnaire (PDHQ) (Vogel-Sprott, 1992). The PDHQ is a self-report measure of alcohol use (see Appendix B1). The PDHQ provided measures of dose (ml of alcohol consumed on an average drinking occasion), weekly frequency of drinking, duration (hours) of a typical drinking session, and drinking rate (dose/duration). The PDHQ also asked if subjects had experienced problems related to their alcohol use. These questions were used to screen out any individuals who reported having experienced problems related to his drinking. However, no subjects reported any such problems.

Placebo manipulation check. At the end of the drinking session, all subjects were asked whether or not they thought that their drinks contained alcohol. If they answered "yes" to this question, then they were asked to estimate the amount of alcohol that they had received in terms of 341ml bottles of 5% beer. Subjects were also asked informally whether or not they thought the alcohol had affected their performance on the tasks. If they reported that their performance on the tasks had been affected, then they were asked to describe the effects.

Procedure

Volunteers were contacted via telephone and were informed as to the nature and requirements of the study before they agreed to participate. The phone script is presented in Appendix B2. All subjects attended a drug-free training session and an alcohol session, separated by no more than seven days.

Drug-free session. At the outset of this session, the nature of the study and requirements were reviewed and subjects read and signed a consent form (Appendix B3). This 45 minute session served to familiarize subjects with the tasks and testing procedure

prior to the administration of any treatment. Their drug-free measures on the tasks performed during this session served to evaluate the adequacy of the LGS and HGS tasks that had been developed and test some assumptions of the race-model of inhibitory control. These data are presented in Appendix B.

Treatment session. Upon arrival for the second session, the experimenter verified that subjects had fasted for 3.5 hours and had taken no alcohol or medication in the previous 24 hours. Only one subject reported not having met these requirements, and the session was rescheduled. Subjects then provided a pre-drinking breath sample to the Breathalyser to familiarize them with the procedure and assure that they were alcohol-free prior to testing. Following the breath sample, subjects were weighed. They completed the PDHQ, and then performed a drug-free test on each of the go-stop tasks in the same order as they had completed them during the drug-free session. Data from these tasks provided drug-free baseline measures to which performance following drinking would be compared. Subjects were then assigned randomly to either an alcohol (A) group (n=8) or to a placebo control (P) group (n=8). The placebo group provided a control for the effect of expecting alcohol.

Subjects assigned to the A group received .62 g/kg of absolute alcohol. This dose was the same as that used by Mulvihill et al. (1997). The alcohol dose was administered in two drinks, mixed in a ratio of one part alcohol to two parts carbonated soft drink (i.e., Wink). Each glass was misted with water prior to serving so that it would appear similar to the placebo drinks.

Subjects assigned to the P group received two placebo drinks consisting of the same carbonated soft drink consumed by the A group. The placebo drinks were equivalent in

volume to the drinks received by the A group. To foster the impression that the placebo drinks contained alcohol, 5 ml of alcohol was floated on the surface of each drink and the glasses were misted with a half-water half-alcohol mixture prior to serving. This mist appeared as condensation and added a strong alcoholic scent to the placebo beverage. This placebo has been used successfully in previous alcohol studies (e.g., Fillmore & Vogel-Sprott, 1995).

Subjects in both groups were given one minute to consume the first drink. Subjects then had a five minute rest followed by the presentation of the second drink, which they also had one minute to consume. This dosage regimen has been found to produce a peak BAC of approximately 70 mg/dL between 60 and 70 minutes following the onset of drinking. Following the second drink, subjects rested until 30 minutes had elapsed from the onset of drinking.

All subjects performed three more tests on the two pairs of go-stop tasks in the same order as they had done prior to drinking. Following the completion of the first test in each pair of tests, subjects rested for one minute before commencing the second test of the pair. An equal number of subjects in each group performed the two tasks in alternate order. The pairs of tests commenced 30, 60, and 90 minutes following the onset of drinking. These test intervals were chosen to coincide with the rising limb, the peak, and the falling limb, respectively, of the blood alcohol curve. Each pair of tests was preceded and was followed by a BAC measure. An additional BAC measure was taken at 70 minutes where the peak BAC was expected. Following the placebo manipulation check, all subjects were debriefed and paid. The second session took approximately 2.25 hours to complete. The time line for the

treatment session is shown in Table 1.

Criterion measures and data analysis. The effects of the treatments were assessed separately on each measure of task performance (i.e., number of inhibitions made and RTGO). This was done by calculating the difference between a subject's score on his drug-free baseline trial and his score on each test following treatment. For example, the effect of treatment on the number of inhibitions displayed on each test of a task was measured by subtracting the number of inhibitions made at baseline by a subject from the number of inhibitions made on each test. A positive change score would indicate improvement in inhibitory control from drug-free baseline because the subject made more inhibitions on the treatment test than on the baseline test. Conversely, a negative score would indicate an impairment in inhibitory control relative to baseline performance. Similarly, the effect of treatment on RTGO was measured by subtracting a subject's RTGO from his baseline test from his RTGO on each treatment test on a task. A negative score indicated that a subject's response to the go-signal was faster on a treatment test than on his baseline test, whereas a positive score indicated that his response was slower on a treatment test than on the baseline test.

The data for each measure on the treatment session were analysed by one-between and two-within factor analyses of variance (ANOVAs) consisting of 2 (groups) X 2 (task load) X 3 (tests). To confirm the results from the difference score analyses the data were also analysed separately for each task load condition by 2 (groups) X 3 (tests) analyses of covariance (ANCOVAs) of a subject's actual test scores, with his drug-free baseline score as a covariate.

Table 1

Time line for the treatment session

-20 minutes	verify study requirements
-19 minutes	breath sample
-18 minutes	PDHQ
-16 minutes	drug-free tests on the pair of LGS and HGS tasks
0-1 minutes	first drink
1-5 minutes	rest
5-6 minutes	second drink
6-30 minutes	rest
30-48 minutes	breath sample and first test on the pair of tasks
48-60 minutes	rest
60-69 minutes	breath sample and second test on the pair of tasks
70 minutes	breath sample
71-79 minutes	second test continued
79-90 minutes	rest
90-108 minutes	breath sample and third test on the pair of tasks
110 minutes	breath sample, manipulation checks, debriefing

Results

Procedural Checks

Subject Characteristics

Subjects' ages, weights, and drinking habit measures from the PDHQ were analysed by one-way analyses of variance (ANOVAs). These analyses revealed no significant group differences (Appendix C1). Individuals in the sample (N=16) had a mean age of 20.88 years (SD=.89) and a mean weight of 78.52 kg (SD=8.35). They reported a mean dose per drinking occasion of 1.22 ml/kg (SD=.53), and a mean weekly frequency of drinking of 1.91 occasions (SD=1.30). The mean duration of a drinking occasion was 3.55 hours (SD=1.54), and the mean drinking rate was .37 ml/kg per hour (SD = .13). These measures of drinking are comparable to those reported for a similar sample of male university students (Chipperfield & Vogel-Sprott, 1984; Vogel-Sprott, 1992).

Baseline performance

Inhibitions. A 2 (group) X 2 (task load) X 4 (stop-signal delay) ANOVA of the number of inhibitions made prior to treatment revealed main effects of task load ($F(1,14)=52.65$, $p<.0001$) and stop-signal delay ($F(3,42)=46.58$, $p<.0001$) (Appendix C2). The main effect of task load confirmed the prediction that more inhibitions should be made on the HGS (mean=28.7) than on the LGS (mean=22.2). The main effect of stop-signal delay indicated that fewer inhibitions were made as the stop-signal delay time increased (see Appendix C2). No effect of group ($F(1,14)=.479$, $p=.500$) was observed and no interactions were significant (ps>.11).

Go-Response RT (RTGO). The response reaction time to the go-signal (RTGO) of the

two groups prior to treatment was tested by a 2 (group) X 2 (task load) ANOVA (Appendix C3). This analysis revealed a main effect of task load ($F(1,14)=92.22$, $p<.0001$), and confirmed that RTGO on the LGS (362.98ms; SD=61.50) was faster than RTGO on the HGS (422.01ms; SD=74.81). No effect of group ($F(1,14)=.908$, $p=.357$) or interaction ($F(1,14)=.720$, $p=.410$) was observed.

A 2 (group) X 2 (task load) ANOVA of response accuracy revealed a main effect of task load ($F(1,14)=6.39$, $p=.024$) (Appendix C3). This indicated that accuracy was somewhat poorer on the HGS (93.79%; SD=5.01) than on the LGS (96.11%; SD=3.65) prior to treatment. However, the response accuracy on both tasks was very high, and the slightly lower accuracy observed on the HGS was consistent with evidence presented in Appendix A and with the notion that the HGS was the more demanding of the two tasks. No main effect of group ($F(1,14)=2.31$, $p=.150$) or interaction ($F(1,14)=.720$, $p=.423$) was observed. Thus. the groups did not differ in response accuracy prior to treatment.

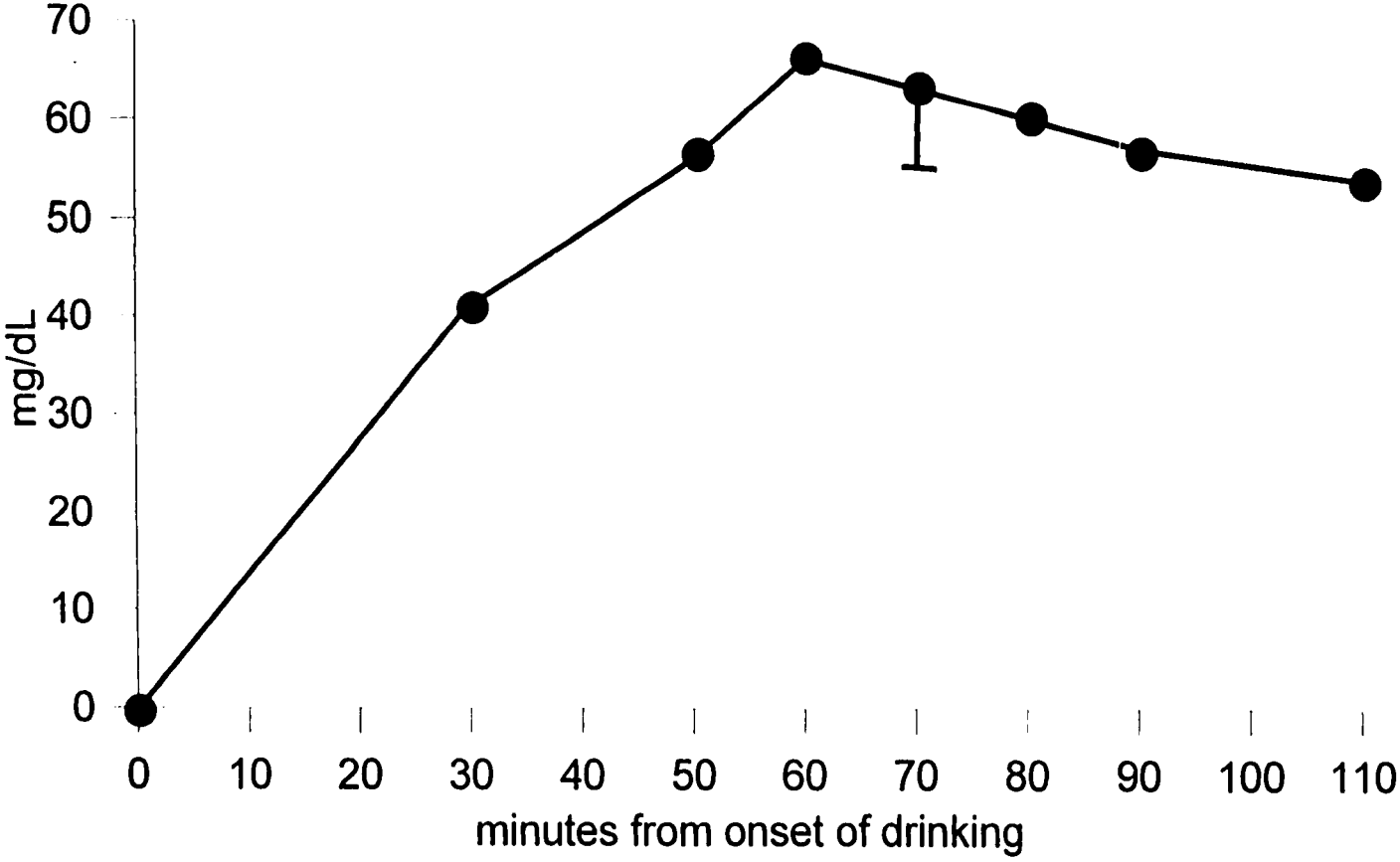
Taken together, the analyses of baseline task performance on both the LGS and HGS tasks showed that the groups did not differ on measures of number of inhibitions made, response reaction time, or response accuracy prior to treatment.

Treatment Effects

A mean peak BAC of 66mg/dL (SD=26) in the A group was observed 60 minutes following the onset of drinking. The mean BACs of the A group during the session are presented in Figure 1. Figure 1 shows that the first pair of tests (30 minutes) occurred on the rising limb of the BAC curve, the second tests (60 minutes) coincided with the peak of the BAC curve, and the third tests (90 minutes) took place on the descending limb of the BAC

Figure 1

Mean BAC of the Alcohol Group during session 2.
Vertical bar shows the largest SEM.



curve.

All subjects in both groups reported that they thought their drinks contained alcohol. Subjects estimated the alcohol that they thought their drinks contained in terms of 341 ml bottles of 5% beer. A one-way ANOVA of these estimates indicated a significant effect of group ($F(1,14)=6.30$, $p=.025$) (Appendix C4). This result showed that the A group estimated their drinks contained more alcohol than did the P group. The mean ratings for the A and P groups were 4.69 (SD=2.42) and 2.13 (SD=1.58) 341 ml bottles of 5% beer, respectively.

Inhibitions. The change in number of inhibitions under the treatments was tested by a 2 (group) X 2 (task load) X 3 (test) ANOVA (Table 2). This analysis obtained main effects of group ($F(1,14)=17.40$, $p=.001$) and test ($F(2,28)=11.08$, $p<.0001$).

Table 2: Analysis of variance of the change score in the number of inhibitions made on three tests on the LGS and HGS tasks by the alcohol and placebo groups:

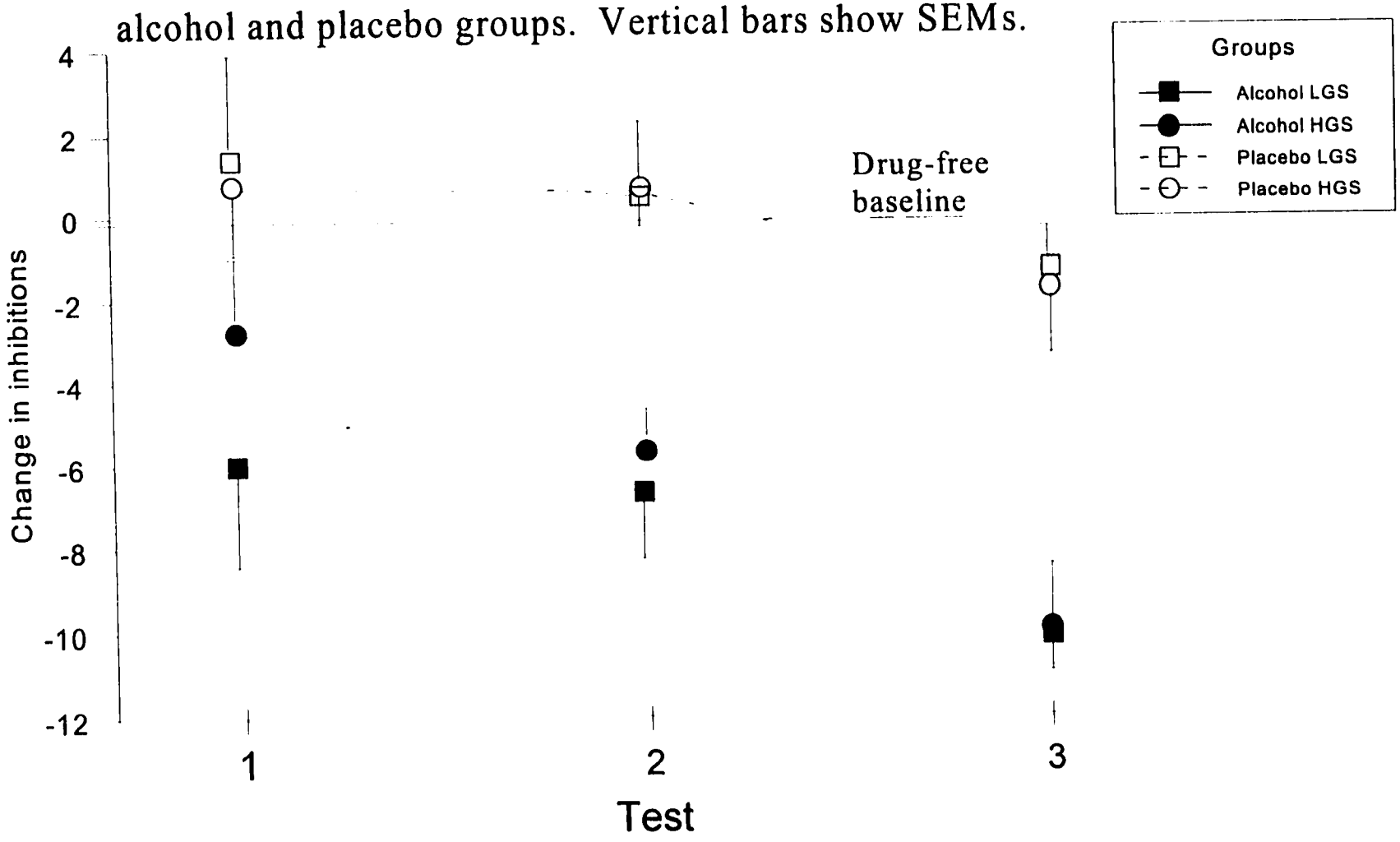
Source	SS	DF	MS	F	p
Between Subjects					
Group (G)	1127.510	1	1127.510	17.396	.001*
Error	907.396	14	64.814		
Within Subjects					
Task Load (L)	7.594	1	7.594	.229	.640
L X G	17.510	1	17.510	.528	.480
Error	464.729	14	33.195		
Test (T)	291.000	2	145.500	11.081	.0001*
T X G	36.333	2	18.167	1.383	.267
Error	367.667	28	13.131		
L X T	9.000	2	4.500	.354	.705
L X T X G	14.333	2	7.167	.563	.576
Error	356.333	28	12.726		

No other effects were significant. Thus, irrespective of the task load, the change in inhibitions differed in the A and P groups and depended upon the test. Figure 2 presents the mean change in inhibitions on the LGS task and the HGS task displayed by the A and P groups on each of the three tests. In Figure 2, zero on the Y-axis represents the drug-free baseline. A negative score indicates fewer inhibitions were made to the 48 stop-signals presented on a test, relative to baseline performance. A positive score indicates that more inhibitions were made. The figure shows that inhibitions were reduced more in the A group than in the P group, and confirms the prediction that alcohol impairs inhibitory control. Post-hoc contrasts indicated that the main effect of test resulted from a greater reduction in inhibitory control by both groups on the tests starting at 90 minutes, relative to the tests at 30 and 60 minutes. The change in inhibitions on the low- and high-load task by the alcohol group was evaluated by a planned comparison using the error term for task load from Table 2 (MS=33.20, df=14). This comparison indicated that the change in inhibitions in the alcohol group did not differ under low- or high-load conditions ($F(1,14)=.14$ $p=.718$). Separate covariance analyses for the LGS and HGS tasks confirmed these findings (Appendix C5).

Go Response RT (RTGO). The change in RTGO under the treatment was tested by a 2 (group) X 2 (task load) X 3 (test) ANOVA (Table 3). This analysis obtained no main effects or interactions (ps>.416). Thus, response reaction times on the tasks did not change significantly across group, task load, or test. These results support the hypothesis that reaction time to the go-signal is not affected significantly by alcohol. The absence of a group X task load interaction is of particular importance because it shows that response time to the go-signal is not affected differently by alcohol on tasks where the time to complete a go-response

Figure 2

Mean change in the number of inhibitions from drug-free baseline on each test on the LGS and HGS tasks by the alcohol and placebo groups. Vertical bars show SEMs.



differs. Covariance analyses, performed separately for the LGS and HGS tasks, supported these findings (Appendix C6).

Table 3: Analysis of variance of the change in response reaction time to the go-signal on three tests of the LGS and HGS tasks by alcohol and placebo groups:

Source	SS	DF	MS	F	p
Between Subjects					
G	2667.115	1	2667.115	.703	.416
Error	53135.808	14	3795.415		
Within Subjects					
L	652.464	1	652.464	.653	.433
L X G	31.228	1	31.228	.031	.862
Error	13992.847	14	999.489		
T	907.360	2	453.680	.883	.425
T X G	1353.578	2	676.789	1.318	.284
Error	14379.760	28	513.563		
L X T	273.020	2	136.510	.613	.549
L X T X G	31.769	2	15.885	.071	.878
Error	6234.548	28	222.662		

Subsidiary analyses

Response accuracy. Measures of response accuracy during tests under alcohol or placebo showed that accuracy remained high on the LGS and HGS tasks. The possibility that accuracy was altered by the treatments was tested by a 2 (group) X 2 (task load) X 3 (test) ANOVA of measures of change in accuracy (Appendix C7). This analysis revealed only a main effect of task load ($F(1,14)=4.69$, $p=.048$), suggesting that the accuracy for both groups decreased slightly more on the LGS (-2.9%; SD=5.7) than on the HGS (-1.0%; SD=4.8)

during testing. No other significant main effects (ps>.217) or interactions (ps>.125) were observed. A covariance analysis for the HGS task also confirmed that the A and P groups did not differ in accuracy (Appendix C8). However, the covariance analysis for the LGS task indicated a group X test interaction ($F(2,28)=3.94$, $p=.031$) (Appendix C8). This interaction was decomposed using simple effects to test the accuracy of the groups at each of the tests. Simple effects on the covariate adjusted means indicated that the A group was slightly less accurate than the P group on the first LGS test following drinking ($F(1,41)=5.47$, $p=.024$). The groups did not differ in accuracy on either of the subsequent LGS tests.

Stop-signal delay. By examining the number of inhibitions made at each stop-signal delay on the go-stop tasks, it was possible to investigate whether or not the pattern of inhibitory control displayed across stop-signal delays was consistent on the LGS and HGS tasks in both the A and P groups. This is of potential interest because theories concerning the effects of alcohol on information processing suggest that deficits in inhibitory control under alcohol should be greater when more information must be processed and when environmental cues are delayed. Thus, in the present study, the effects of alcohol on inhibitory control on both the low- and high-load tasks should be least evident at the earlier stop-signal delays, and greatest on the later stop-signal delays.

An exploratory analysis of the change in inhibitions at each stop-signal delay was conducted (Table 4). This 2 (group) X 2 (task load) X 3 (test) X 4 (stop-signal delay) ANOVA revealed a significant three-way interaction involving group, task load, and delay ($F(3,42)=6.61$, $p=.001$), as well as the significant main effects of groups and tests reported in Table 1. Figure 3 shows the mean change in inhibitions to the 10 stop-signals at each delay

Table 4: Analysis of variance of the change in number of inhibitions made at each stop-signal delay on each of three tests on both the LGS and HGS tasks by the alcohol and placebo groups:

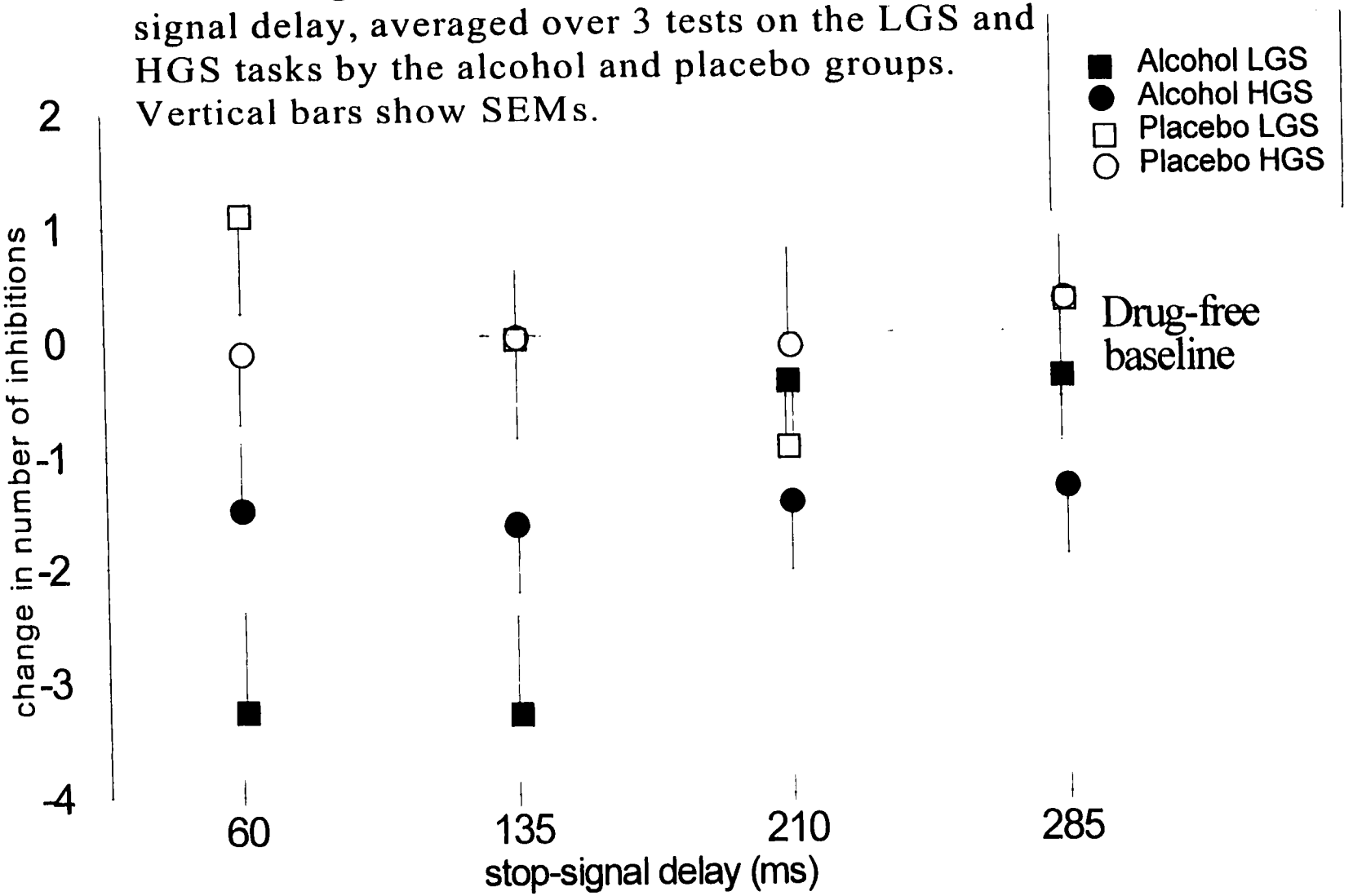
Source	SS	DF	MS	F	p
Between Subjects					
G	265.003	1	265.003	17.003	.001*
Error	218.203	14	15.586		
Within Subjects					
L	.753	1	.753	.106	.749
L X G	2.503	1	2.503	.353	.562
Error	99.203	14	7.086		
T	76.396	2	38.198	12.365	.0001*
T X G	10.021	2	5.010	1.622	.216
Error	86.500	28	3.089		
D	42.284	3	14.095	1.324	.279
D X G	91.013	3	30.338	2.851	.049*
Error	446.995	42	10.643		
L X T	2.771	2	1.385	.371	.693
L X T X G	5.146	2	2.573	.689	.510
Error	104.500	28	3.732		
L X D	17.263	3	5.754	1.291	.290
L X D X G	88.451	3	29.484	6.613	.001*
Error	187.245	42	4.458		
T X D	14.146	6	2.358	1.135	.349
T X D X G	13.479	6	2.247	1.082	.380
Error	174.458	84	2.077		
L X T X D	13.854	6	2.309	1.383	.231
L X T X D X G	5.854	6	.976	.585	.742
Error	140.208	84	1.669		

for the A and P groups on the LGS task and the HGS task. The figure indicates that the interaction resulted because the A group showed considerable impairment of inhibitory control on the LGS task at the early stop-signal delays (60 and 135 ms), but not at the later stop-signal delays (210 and 285 ms). Conversely, on the HGS task, the A group showed fairly consistent impairment in inhibitory control across all delays. Appendix C9 shows the change in inhibitions and the covariate adjusted mean number of inhibitions made at each stop-signal delay on the LGS and HGS tasks for the A and P groups. The P group performed similarly to their drug-free performance at each stop-signal delay on both tasks (see Figure 3). This interpretation was tested by conducting two separate 2 (group) X 4 (stop-signal delay) ANOVAs on the change in inhibitions on each task condition (Appendix C10). On the LGS task, the ANOVA revealed a significant group X stop-signal delay interaction ($F(1,14)=9.73$, $p=.008$), indicating that relative to the P group the A group was impaired at the early delays, but not at the later delays. On the HGS task, the analysis revealed only a main effect of group ($F(1,14)=17.45$, $p=.001$), indicating a constant disruption in inhibitory control across all stop-signal delays in the A group relative to the P group.

The possibility that the group X task load X delay interaction might have resulted from a floor effect at the longest delay (285ms) was tested by a four-way ANOVA of the change in inhibitions using only the three earliest delays (60, 135, and 210 ms) (Appendix C11). The results from this analysis were consistent with the results from the original analysis, indicating a main effect of group ($p=.001$), a main effect of test ($p<.0001$), and a group X task load X stop-signal delay interaction ($p=.003$). Thus, these results indicated that the difference in the pattern of impaired inhibitory control on the LGS and HGS displayed under a moderate dose

Figure 3

Mean change in number of inhibitions at each stop-signal delay, averaged over 3 tests on the LGS and HGS tasks by the alcohol and placebo groups. Vertical bars show SEMs.



of alcohol could not be attributed to a floor effect at the longest stop-signal delay.

Discussion

The evidence indicated that a moderate dose of alcohol can selectively disrupt the inhibitory control displayed by social drinkers on go-stop tasks. Relative to their drug-free performance, subjects who received a moderate dose of alcohol were less able to inhibit a go-response when it was a followed by a stop-signal than were subjects who received a placebo. Results from this study also showed that the overall degree of impairment in inhibitory control displayed under a moderate dose of alcohol was not affected by increasing the processing demands required to complete a go-response. The evidence revealed that alcohol did not significantly change response reaction time to the go-signal, and had little effect on response accuracy displayed during testing. Furthermore, the inhibitory control displayed during testing under alcohol did not appear to depend on the blood alcohol concentration at the time of testing, as the degree of impairment was consistent across the test intervals. This is inconsistent with findings from motor skills tasks where the greatest impairment under alcohol is typically observed at the peak BAC.

Although the overall degree of impairment of inhibitory control did not appear to be affected by the processing load of the task, exploratory analyses indicated that the degree of impairment displayed to the stop-signal delays under alcohol differed on the low-load and high-load go-stop tasks. The reduction in the number of inhibitions displayed under alcohol was fairly consistent across all stop-signal delays on the high-load go-stop task, whereas impairment on the low-load go-stop task was evident only at the earlier delays. These preliminary findings are of interest because they seem inconsistent with a "myopia" theory of

the effect of alcohol, which would predict that responses to more proximal cues should be less affected by the drug. Accordingly, the impairment in inhibitory control should have been greater at the longer stop-signal delays on both low- and high-load go-stop tasks.

The finding that greater impairment of inhibitory control was displayed at the shorter stop-signal delays on a simple task is also somewhat inconsistent with the notion that the effects of alcohol are greater when cues for responding require more processing. This finding would have to be replicated to be verified. One possible interpretation of this finding is that when little processing is required to respond to a go-response, as in the low-load go-stop task, alcohol might reduce the ability to process new stop-signal information that is presented close in time to the go-signal. If this is the case, then inhibitory control under alcohol should be more impaired when the go-signal and the stop-signal are presented simultaneously in the low-load task. Thus, the greatest impairment in inhibitory control under alcohol should be observed at a stop-signal delay of 0ms. This prediction will be tested in Study 2.

In summary, the results of Study 1 indicated that a moderate dose of alcohol can disrupt inhibitory control on cognitive tasks, without significantly affecting response reaction time or response accuracy. The data further suggest that the overall degree to which inhibitory control is impaired under alcohol is not affected by increasing the time to complete the go-response of a task.

ALCOHOL STUDY 2

This experiment was designed to test the effect of alcohol on the ability to inhibit and to switch a response following the presentation of a stop-signal. Stopping one activity and switching to another is also termed "response reengagement" or "response flexibility" and is thought to be integral to the executive cognitive processes that characterize cognitive flexibility (Lezak, 1983). Lesion studies have noted that the inability to change from one response to another, or from one line of thought to another, is often accompanied by a lack of inhibitory control, and that both processes are often compromised following damage to the frontal areas (Petrides & Milner, 1982). Study 1 indicated that a moderate dose of alcohol reduced inhibitory control. Study 2 investigated whether or not the impairment in inhibitory control under alcohol was also accompanied by an impairment in response flexibility.

Research testing the ability to reengage a second response following inhibition of a first response has used a change-paradigm (Logan & Burkell, 1986). The change paradigm is a variation of the go-stop paradigm where, in addition to responding to go-signals and withholding responses to stop-signals, subjects are required to make a different response following the presentation of the stop-signal. Thus, the change paradigm measures the reaction time to go-signals, the inhibitions to stop-signals, and the reaction time to make a second response after inhibitions and failures to inhibit. Basic research using the change paradigm has observed that the response time of the second response is longer on trials when subjects failed to inhibit their response than on trials when an inhibition was made (Logan & Burkell, 1986). This evidence indicated that making a first response interfered with making a second response, suggesting that the change paradigm measures competition within the

response system (Logan & Burkell, 1986, p554).

The change paradigm has been used to evaluate the ability to reengage a response displayed by individuals with clinically diagnosed deficits in inhibitory control. For instance, relative to age-matched controls, children with ADHD have been found to demonstrate significantly slower and more variable response reengagement (Schachar, Tannock, Marriott, & Logan, 1995). Using a placebo-control design, deficits in the response reengagement of ADHD children were reduced following the administration of methylphenidate (Tannock, Schachar, & Logan, 1995).

The application of the change paradigm to behaviour under alcohol is of theoretical and practical interest. From a theoretical perspective, it has been argued that the executive processes referred to as "cognitive flexibility" include the ability to switch from one response to another. The literature reviewed concerning the effects of an acute dose of alcohol on brain metabolism suggested that alcohol has a preferential effect on the frontal cortices. If executive cognitive processes require intact frontal lobe function, as is implied by the neuropsychological literature, then response reengagement might also be disrupted by an acute dose of alcohol.

If alcohol interferes with the response flexibility, then the reaction time of a second response (RT2) should be slower under alcohol than under drug-free conditions. As reaction time for the second response has been found to be slower following failures to inhibit (RT2 fail) than following inhibitions (RT2 inhibit) of a first response, the effect of alcohol on RT2 will be examined separately for inhibitions and failures to inhibit.

In addition to the main hypothesis, this study was designed to determine whether or

not the effect of alcohol on inhibitions and RTGO observed on the low- and high-load go-stop tasks in Study 1 also applied to low- and high-load change tasks whose development is reported in Appendix D. Specifically, a moderate dose of alcohol should reduce the number of inhibitions to a similar degree on low- and high-load change tasks, and the reaction time to go-signals should be unaffected.

This study also examined the intensity of alcohol-induced impairment of inhibitory control as a function of stop-signal delays on the low- and high-load change tasks. Alcohol Study 1 had indicated that the reduction in inhibitions under alcohol was similar at all stop-signal delays when the high-load go-stop task was performed, but impairment on the low-load go-stop task was only evident at the shorter (i.e., 60 and 135ms) stop-signal delays. The two go-stop tasks only differed in terms of high versus low cognitive load go-signals. Thus the different pattern of alcohol-induced impairment at stop-signal delays on the two tasks might be due to the low- and high-load go-signals. If this is the case, these two different patterns might also be evident when low- and high-load change tasks are performed under alcohol.

The study also explored the suggestion that when little processing is required to respond to a go-signal, alcohol might interfere with processing new stop-signal information. If this is the case, then the inhibitory control displayed under alcohol should be most impaired when the go- and stop-signals occur simultaneously. To further investigate this possibility, an additional stop-signal delay was presented at the same time as the go-signal (i.e., 0ms) in both change tasks in the present study.

Method

Subjects

Sixteen right-handed males, age 19-23, were recruited from the University of Waterloo Cognitive Subject Pool. Subjects were healthy social-drinkers who were not taking either prescription or over-the-counter medication at the time of the study. Subjects agreed to fast for 3.5 hours prior to the treatment session, and received $15 for their participation in the study. Ethical approval for this research project was obtained from the University of Waterloo Office of Human Research.

Apparatus

Tasks. Performance was measured on two change tasks (low-load and high-load). All tasks were programmed using Micro Experimental Laboratory (MEL), version 2.0, software (Pittsburgh, PA., 1995). Tasks were run using a 386/33 PC.

(1) Low-load change task (LC): This task used the low-load go-signals that were employed in the low-load go-stop task in Alcohol Study 1. Subjects were required to discriminate between an "X" and "O", presented one at a time, by using the index and middle fingers of their right hand to press one of two keys on a keyboard. If "X" appeared, then the right key was pressed; if "O" appeared, then the left key was pressed. Each subject was seated 60 cm from the computer screen. The presentation of each letter was preceded by a preparatory fixation point (.) for 500 ms. Each letter was 1 cm in height and .5 cm in width and was presented at the centre of the computer screen for 500 ms. Subjects were instructed to respond as quickly and as accurately as possible.

Subjects were also told to try to withhold their response whenever a go-signal was followed by a stop-signal. The stop-signal was a 900 Hz tone presented for 500 ms following the onset of the go-signal. Stop-signals were presented infrequently (on approximately 28.4%

of trials) and in a pseudo-random order, with no more than three stop-signals occurring in succession. In addition to the four stop-signal delays presented in Study 1, a stop-signal delay that occurred at the same time as the go-signal (i.e., 0 ms) was included. Thus, an equal number of stop-signals was presented at 0, 60, 135, 210, and 285 ms following the onset of the go-signal.

The ability to switch a response following a stop-signal, or "response flexibility", was assessed by requiring subjects to make a different response whenever a stop-signal occurred. Subjects made this response by using the index finger of their left hand to press a key on the computer keyboard. They were instructed to respond on this key as quickly as possible whenever a stop-signal occurred. Response flexibility was measured by the reaction time of this second response (RT2) when subjects inhibited to the stop-signal (RT2 inhibit) and when subjects failed to inhibit their response to the stop-signal (RT2 fail).

Each letter presentation constituted one trial, and trials were separated by 1.5 sec. One test consisted of 176 trials. Each test was presented in two blocks of 88 trials, separated by a 30 second rest period. Each test included 50 stop-signals, with 10 stop-signals at each of the five delay intervals. These stop-signals necessitated a response with the left hand. A block took 3 minutes and 45 seconds to complete and a test took 7 minutes and 45 seconds to complete.

(2) High-load change task (HC): This task was identical to the LC task, except that the target letters ("X" and "O") were presented along with five distracter letters (R, S, T, B, N) in a horizontal string in the centre of the computer screen . The order of the letters in each string was varied pseudo-randomly. Each of the target letters ("X" and "O") appeared 15

times in the first, second, third, and fourth positions, and 14 times in each of the fifth and sixth positions of the letter strings in each test. One target letter was present on each trial.

Within each test, the 10 stop-signals at each delay were evenly distributed across each target letter (i.e., with five stop-signals at each delay for both "X" and "O" target trials). A stop-signal at a given delay interval never appeared more than once at a given string location during a test.

The LC and HC tasks also provided measures of the number of inhibitions at each stop-signal delay and the total number of inhibitions made by a subject on each test, as well as reaction time to the go signal when no stop-signal was present (RTGO). The reaction time of response flexibility was measured when subjects inhibited (RT2 inhibit) and failed to inhibit (RT2 fail) their response to the stop-signal.

The accuracy of the go-response continued to be monitored by measuring the percentage of times the subject pressed the correct key in response to a go-stimulus when no stop-signal was present. Each subject performed the task alone in a room. The presentation of stimuli and recording of data were controlled by the computer.

Blood alcohol concentrations (BACs). BACs were measured from breath samples using a Stephenson Model 900A Breathalyser.

Drinking habits. Subjects filled out the Personal Drinking History Questionnaire (PDHQ) (Vogel-Sprott, 1992). The measures of this questionnaire are described in Study 1.

Placebo manipulation check. At the end of the drinking session, all subjects were asked whether or not they thought that their drinks contained alcohol. If they answered "yes" to this question, then they were asked to estimate the amount of alcohol that they had received

in terms of 341ml bottles of 5% beer. Subjects were also asked informally whether or not they thought the alcohol had affected their performance on the tasks. If they reported that their performance on the tasks had been affected, then they were asked to describe the effects.

Procedure

The procedure for this study was identical to that of Study 1. All subjects were contacted via telephone and attended a drug-free familiarisation session and a treatment session.

Drug-free session. At the outset of this session, the nature of the study and requirements were reviewed and subjects read and signed a consent form. This 45 minute session served to familiarize subjects with the tasks and testing procedure. Task instructions are shown in Appendix D1. This session was also designed to compare subjects' drug-free performance on the go-stop tasks used in Study 1 and the change tasks used in Study 2. The rationale for, and results of, these drug-free tests are presented in Appendix D.

Treatment session. Subjects provided a pre-drinking breath sample and filled out the PDHQ. They then performed a drug-free baseline test on each of the change tasks in the same counterbalanced order as they had completed them during the drug-free session. An equal number of subjects who performed the two tasks in the same order were randomly assigned to either an alcohol (A) group (n=8) or to a placebo (P) group (n=8). The placebo group provided a control for the effect of expecting alcohol.

The schedule of events during the treatment session was identical to the time line of Study 1 (see Table 1). Subjects in the A group received .62 g/kg of absolute alcohol, mixed in a ratio of one part alcohol to two parts carbonated soft drink, and administered in two drinks.

The P group received carbonated beverage equivalent in volume to that administered to the A group, and with 5 ml of alcohol floated on the surface of each drink.

All subjects were given one minute to finish the first drink. After a 5 minute rest, they received a second drink that was also consumed in one minute. Thirty minutes after the onset of drinking, all subjects gave a breath sample and performed the first test on the pair of tasks in the same counterbalanced order as the drug-free baseline. All subjects performed additional pairs of tests at 60 and 90 minutes following the onset of drinking and gave breath samples throughout the session.

Criterion measures and data analysis. The effects of the treatments were assessed separately on each measure of task performance. Treatment effects were measured by the difference between a subject's score on his drug-free baseline trial and his score on each test under treatment. For example, the effect of treatment on the reaction time of the second response following an inhibition (RT2 inhibit) was measured by subtracting a subject's RT2 (inhibit) made on the baseline test from his RT2 (inhibit) on each treatment test. A positive change score indicated that RT2 (inhibit) had slowed from drug-free baseline and a negative score indicated that RT2 (inhibit) was faster. Similar difference scores were calculated for RT2 (fail), as well as number of inhibitions, and RTGO. The resulting difference scores for each measure were analyzed by one-between and two-within factor ANOVAs consisting of 2 (groups) X 2 (task load) X 3 (tests). To confirm the results from the analysis of difference scores, the data for each measure were also analysed separately for each task load condition by 2 (groups) X 3 (tests) ANCOVAs of a subject's actual test scores, using his drug-free baseline score as a covariate.

Results

Procedural Checks

Subject Characteristics

Subjects' ages, weights, and drinking habit measures from the PDHQ were analyzed. One-way analyses of variance (ANOVAs) for each measure found no significant group differences (Appendix E1). Individuals in the sample (N=16) had a mean age of 20.81 years (SD=1.47) and a mean weight of 77.29 kg (SD=12.91). They reported a mean dose per drinking occasion of 1.26 (SD=.52) ml alcohol/kg, and a mean weekly frequency of drinking of 1.97 (SD=1.70). The mean duration of a drinking occasion was 3.78 hours (SD=1.72), and the mean drinking rate was .43 (SD=.40) ml alcohol/kg per hour. These measures of drinking are comparable to those reported in Alcohol Study 1.

Baseline performance

Response Flexibility (RT2). A 2 (group) X 2 (task load) X 2 (flexibility) ANOVA of RT2 indicated a significant task load X flexibility interaction ($F(1,14)=10.47$, $p=.006$) (Appendix E2). Tests of simple effects indicated that this interaction resulted because the RT2 (inhibit) did not differ on the two tasks (LC=403.55ms, SD=50.05; HC=406.10ms, SD=66.64). In contrast, the RT2 (fail) was slower on the HC task (478.73ms; SD=84.44) than on the LC task (431.88ms; SD=80.02). These findings confirm that a failure to inhibit a response reduces flexibility by slowing the reaction time of a second response, and that this effect is greater on a task presenting go-signals that require more processing.

Inhibitions. A 2 (group) X 2 (task load) X 5 (stop-signal delay) ANOVA of the number of inhibitions made prior to treatment revealed a main effect of task load

($F(1,14)=18.58$, $p=.001$) and a main effect of stop-signal delay ($F(4,56)=58.32$, $p=.0001$) (Appendix E3). The main effect of task load confirmed that more inhibitions were made on the HC (30.6; SD=9.7) than on the LC (24.6; SD=8.7). The mean number of inhibitions at each stop-signal delay on the LC and HC tasks are shown in Appendix Table E3. These means indicate that the main effect of stop-signal delay reflected a systematic reduction in inhibitions as delay time increased. No effect of group ($F(1,14)=.001$, $p=.978$) was observed and no interactions were significant (ps>.107). Thus the number of inhibitions made by the groups did not differ prior to treatment.

Go-Response RT (RTGO). A 2 (group) X 2 (task load) ANOVA of RTGO on the baseline test of the two change tasks revealed a main effect of task load ($F(1,14)=120.49$, $p<.0001$), and confirmed that RTGO on the LC (387.96ms; SD=47.08) was faster than RTGO on the HC (472.94ms; SD=61.84) (Appendix E4). No other effects were significant (ps>.660).

A 2 (group) X 2 (task load) ANOVA of response accuracy revealed a main effect of load ($F(1,14)=13.73$, $p=.002$), indicating that accuracy was slightly poorer on the HC (95.19%; SD=3.43) than on the LC (97.06%; SD=2.44) prior to treatment (Appendix E4). This result confirmed the finding from Study 1 that performance on a low-load task is slightly more accurate than performance on the more demanding high-load task.

In summary, the analyses of baseline performance on the low- and high-load change tasks indicated that the groups did not differ on measures of inhibitory control, response flexibility, go-signal RT, or response accuracy prior to treatment.

Treatment Effects

A mean peak BAC of 73mg/dL (SD=10) in the A group was observed 70 minutes following the onset of drinking. The mean BACs of the A group at intervals during the session are presented in Figure 4. Figure 4 shows that the first pair of tests (30 minutes) occurred on the rising limb of the BAC curve, the second pair (60 minutes) coincided with the peak of the BAC curve, and the third pair (90 minutes) took place on the descending limb of the blood alcohol curve.

All subjects reported that their drinks contained alcohol. A one-way ANOVA tested the amount of alcohol subjects reported they had received (Appendix E5). This analysis revealed a significant effect of group ($F(1,14)=10.94$, $p=.005$), indicating that the A group (4.63 bottles of beer; SD=1.81) estimated that their drinks contained more alcohol than did the P group (2.25 bottles; SD=.93).

Response Flexibility (RT2). The change in response flexibility (RT2 inhibit and RT2 fail) under the treatments was tested by a 2 (group) X 2 (task load) X 2 (flexibility) X 3 (test) ANOVA of RT2 (Table 5). This analysis revealed a group X flexibility interaction ($F(1,14)=5.78$, $p=.031$) and a task load X flexibility interaction ($F(1,14)=6.48$, $p=.023$).

The group X flexibility interaction is illustrated in Figure 5, which shows the mean change from baseline in RT2 following inhibitions and failures to inhibit on both tasks by the alcohol and placebo groups. A positive score indicates that RT2 was slower during treatment tests than at baseline, and a negative score indicates that RT2 was faster. Figure 5 shows that the change from baseline in RT2 following inhibitions did not differ in the A group (-15.80ms; SD=47.03) or P group (-10.18ms; SD=45.65). In contrast, RT2 following a failure to inhibit slowed in the A group (+34.73ms; SD=64.08) and sped up in the P group (-27.56ms;

Figure 4

Mean BAC of the Alcohol Group during session 2.
Vertical bar shows largest SEM.

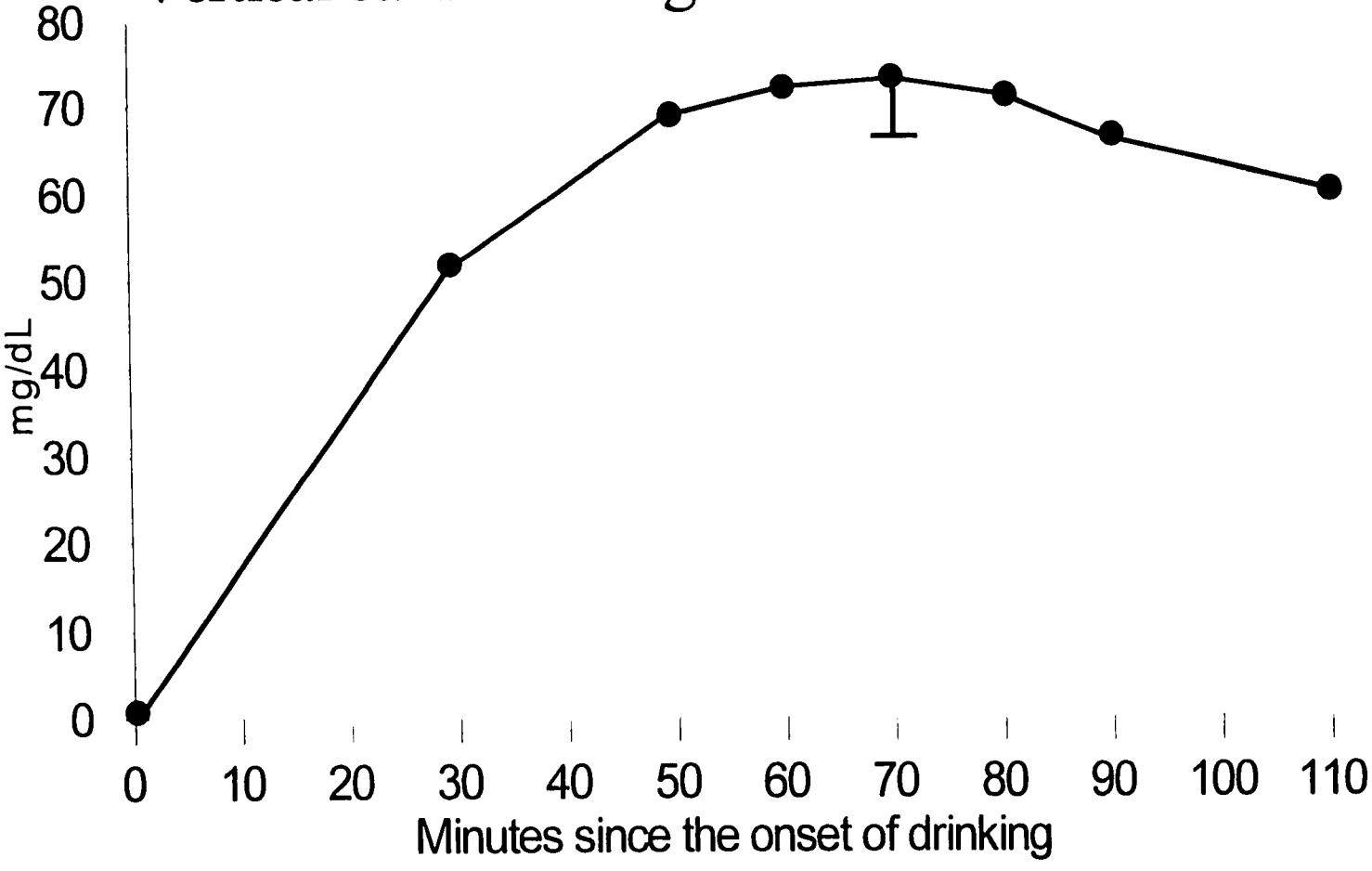
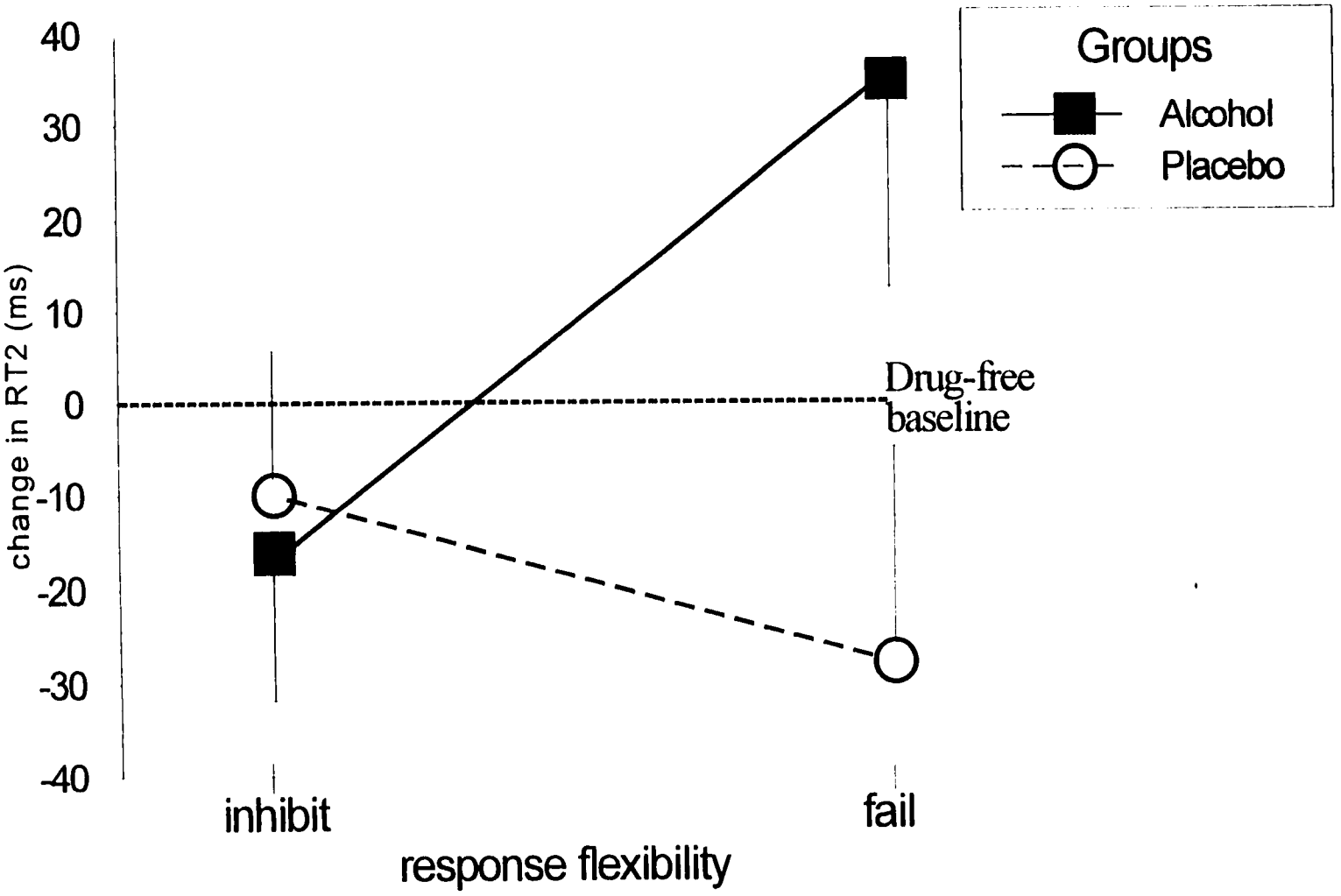


Table 5: Analysis of variance of the change in flexibility (RT2) on three tests on the low-load and high-load change tasks by the alcohol and placebo groups:

Source	SS	DF	MS	F	p
Between Groups					
G	38539.567	1	38539.567	2.041	.175
Error	264389.886	14	18884.992		
Within Groups					
L	599.324	1	599.324	.096	.761
L X G	2203.366	1	2203.366	.353	.562
Error	87411.530	14	6243.681		
Flexibility (F)	13197.017	1	13197.017	1.379	.260
F X G	55342.575	1	55342.575	5.782	.031*
Error	133999.812	14	9571.415		
T	3112.278	2	1556.139	1.418	.259
T X G	2312.672	2	1156.336	1.054	.362
Error	30723.813	28	1097.279		
L X F	13089.789	1	13089.789	6.475	.023*
L X F X G	868.361	1	868.361	.430	.523
Error	28302.611	14	2021.615		
L X T	555.187	2	277.593	.253	.778
L X T X G	2713.232	2	1356.616	1.235	.306
Error	30754.165	28	1098.363		
F X T	3596.950	2	1798.475	1.944	.162
F X T X G	1189.134	2	594.567	.643	.533
Error	25903.689	28	925.132		
L X F X T	2220.921	2	1110.461	1.764	.190
L X F X T X G	328.231	2	164.116	.261	.772
Error	17626.246	28	629.509		

Figure 5

Change in response flexibility following inhibitions and failures to inhibit. Vertical bars show SEMs.



SD=55.59). Thus, alcohol impaired response flexibility following a failure to inhibit a first response and appeared to have little effect on response flexibility when the first response was inhibited. Separate covariance analyses on RT2 (inhibit) and RT2 (fail) on both the LC and HC were in line these findings (Appendix E6). The adjusted means from these analyses indicated that RT2 (inhibit) on both tasks did not differ in the A and P groups, whereas RT2 (fail) tended to be slower in the A group than in the P group.

The task load X flexibility interaction is shown in Figure 6, and indicates that the change in RT2 (inhibit) (-6.50ms; SD=48.67) and RT2 (fail) (-6.43ms; SD=66.83) did not differ on the HC task. However, on the LC task, RT2 (inhibit) was slightly faster during treatment (-19.48ms; SD=42.45), whereas RT2 (fail) was slightly slower during treatment (+13.61ms; SD=70.31).

Inhibitions. The change in number of inhibitions under the treatments was tested by a 2 (group) X 2 (task load) X 3 (test) ANOVA (Table 6). This analysis revealed only a main effect of group ($F(1,14)=11.76$, $p=.004$). Figure 7 shows the mean change in inhibitions to the 50 stop-signals, averaged over treatment tests on the LC and HC tasks in the A and P groups. A positive score indicates that inhibitions increased under treatment, whereas a negative score indicates that fewer inhibitions were made. The figure shows that the A group made fewer inhibitions following treatment than the P group, and confirms the prediction that alcohol impairs inhibitory control. The change in inhibitions on the low- and high-load task by the alcohol group was evaluated by a planned comparison using the error term for task load from Table 6 (MS=52.64, df=14). This comparison indicated that the change in inhibitions in the alcohol group did not differ under low- or high-load conditions ($F(1,14)=1.12$, $p=.309$).

Figure 6

Change in response flexibility following inhibitions and failures to inhibit on low-load and high-load change tasks. Vertical bars show SEMs.

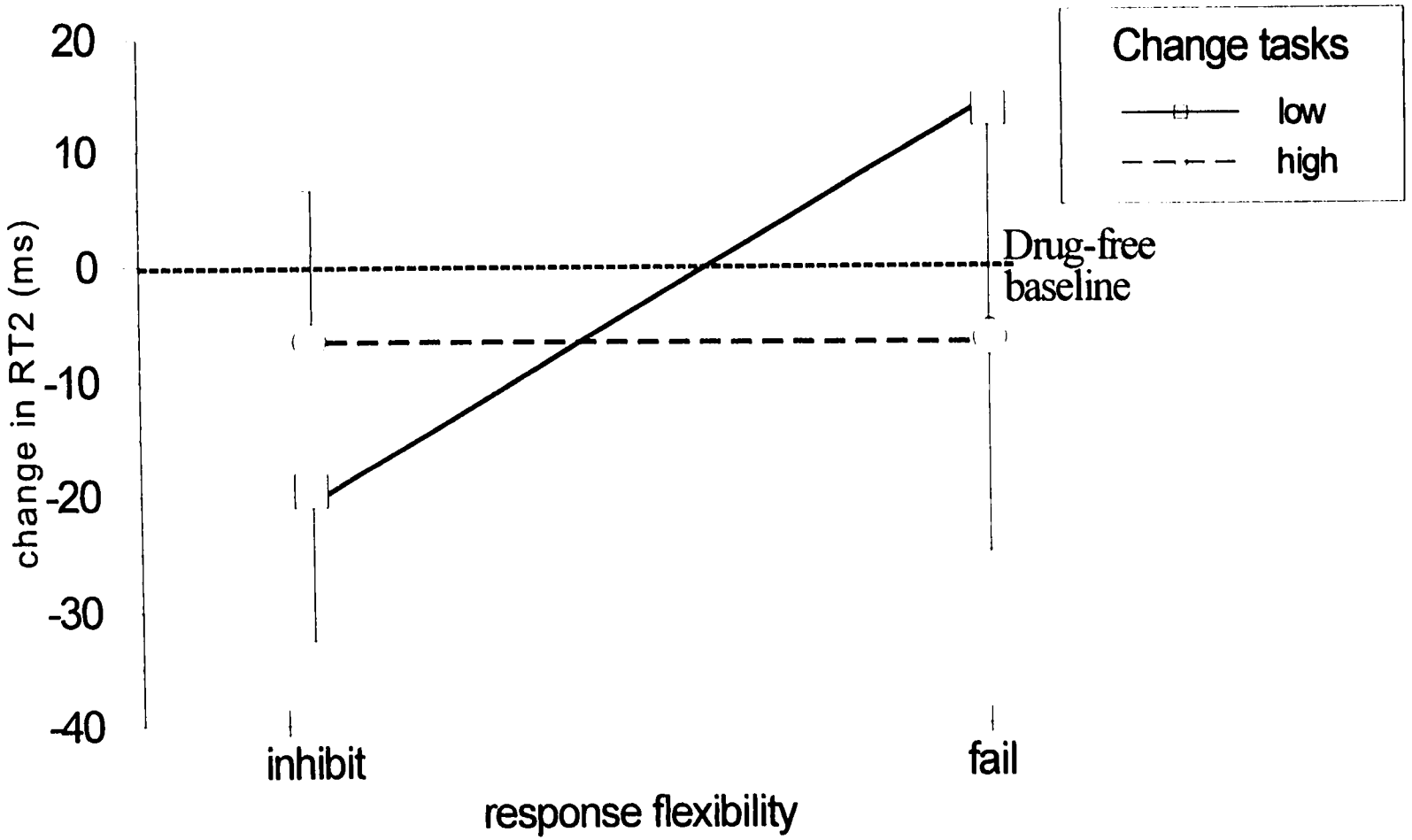
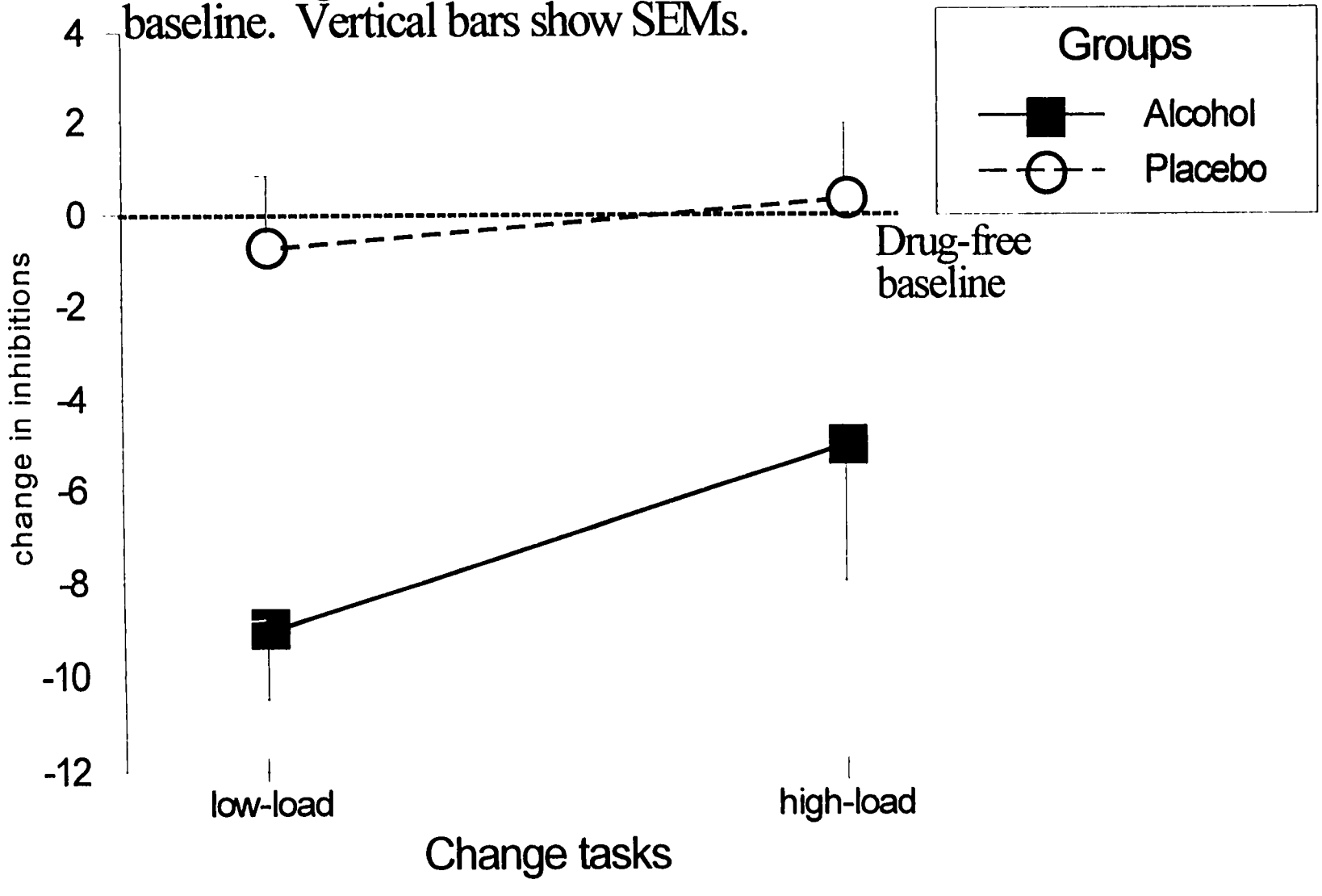


Table 6: Analysis of variance of the change in the number of inhibitions made on three tests of the LC and HC tasks by the alcohol and placebo groups:

Source	SS	DF	MS	F	p
Between Subjects					
G	1162.042	1	1162.042	11.755	.004*
Error	1383.917	14	98.851		
Within Subjects					
L	150.000	1	150.000	2.849	.114
L X G	42.667	1	42.667	.810	.383
Error	737.000	14	52.643		
T	7.937	2	3.969	.287	.753
T X G	.146	2	.073	.005	.995
Error	387.583	28	13.842		
L X T	28.938	2	14.469	1.265	.298
L X T X G	13.146	2	6.573	.575	.569
Error	320.250	28	11.438		

Figure 7

Mean change in number of inhibitions from drug-free baseline. Vertical bars show SEMs.



The results of separate covariance analyses for the LC and HC tasks were consistent with the conclusion that alcohol impaired inhibitory control (Appendix E7), and indicated that the impairing effect on the HC task was not as strong as that on the LC task.

Go-Response RT (RTGO). The effect of treatment on RTGO was tested by a 2 (group) X 2 (task load) X 3 (test) ANOVA (Table 7). This analysis indicated no significant main effects or interactions. These results support the hypothesis that reaction time to the go-signal is not significantly changed by alcohol. Separate analyses of covariance for the LC and HC tasks confirmed the conclusion that RTGO did not differ between the groups (Appendix E8). A main effect of test approached significance in the analysis of the LC task ($F(2,28)=3.01$, $p=.065$), indicating that RTGO slowed slightly under alcohol and placebo as testing progressed.

Subsidiary analyses

Response accuracy. The effect of treatment on the change in response accuracy of both tasks was tested by a 2 (group) X 2 (task load) X 3 (test) ANOVA of the change in accuracy (Appendix E9). This analysis revealed a significant three-way interaction of group X task load X test ($F(2,28)=4.47$, $p=.021$). Separate 2 (group) X 3 (test) ANOVAs of the change in response accuracy for both tasks were run to clarify this effect (Appendix E10). The analysis for the LC task indicated main effects of group ($F(1,14)=10.30$, $p=.006$) and test ($F(2,28)=3.30$, $p=.052$). The main effect of group indicated that the A group was slightly less accurate across the tests. The main effect of tests resulted because accuracy was slightly better on the final test (90 minutes) than on the two earlier tests (30, 60 minutes). The analysis for the HC task indicated a test X group interaction ($F(2,28)=4.34$, $p=.023$). This

Table 7: Analysis of variance of the change in response reaction time to the go-signal on three tests of the LC and HC tasks by the alcohol and placebo groups:

Source	SS	DF	MS	F	p
Between Subjects					
G	5135.423	1	5135.423	1.691	.214
Error	42513.192	14	3036.657		
Within Subjects					
L	96.120	1	96.120	.182	.676
L X G	762.641	1	762.641	1.447	.249
Error	7379.943	14	527.139		
T	2131.317	2	1065.659	2.502	.100
T X G	2237.841	2	1118.921	2.627	.090
Error	11927.982	28	425.999		
L X T	171.004	2	85.502	.405	.671
L X T X G	10.972	2	5.486	.026	.974
Error	5914.332	28	211.226		

interaction resulted because the A group was less accurate than the P group on the second test, but not on the first or third tests. However, the overall adjusted mean accuracy of the A group (93.9%) was only slightly less than that of the P group (95.9%), and the slight difference in accuracy varied in a rather unpredictable fashion depending on the task load and particular test.

Stop-signal delay: The change in number of inhibitions from baseline made at each stop-signal delay was evaluated by a 2 (group) X 2 (task load) X 3 (test) X 5 (stop-signal delay) ANOVA (Appendix E11). Apart from the main effect of group (also shown in Table 6), this analysis revealed no other main effects or interactions (ps>.108). A set of three

planned comparisons evaluated the hypothesis that the greatest reduction in inhibitions under alcohol would be displayed at the earlier delays (Appendix E12), especially on the LC task. These comparisons evaluated the change in number of inhibitions of the A group separately for the LC and HC tasks at (1) the shortest (0ms) stop-signal delay versus all other delays, (2) the two shortest (0ms and 60ms) stop-signal delays versus all other stop-signal delays, and (3) the first, second, and third stop-signal delays against the remaining delays. These comparisons indicated a trend for the greatest reduction in inhibitions under alcohol at the shortest stop-signal delay (i.e., 0ms) on the LC task ($F(1,7)=4.33$, $p=.038$, one-tailed). However, no other comparisons reached significance (all $ps>.205$), suggesting that the deficits in inhibitory control elicited under alcohol on both the change tasks were quite consistent across all other stop-signal delays. The change in the number of inhibitions and the actual number of inhibitions made at each stop-signal delay on the low- and high-load tasks by the A and P groups are shown in Appendix E13.

Discussion

The evidence from this study confirmed that a moderate dose of alcohol can disrupt inhibitory control to a similar degree on low- and high-load change tasks performed by social drinkers, without affecting response reaction time to go-signals. By using change tasks, the experiment also tested the effects of alcohol on response flexibility. The findings showed that the drug slowed the reaction time to make a second response following a failure to inhibit a first response, and this effect did not differ on change tasks that presented low- or high-load go-signals. Although response accuracy remained high for the alcohol group, some evidence indicated that accuracy decreased slightly during treatment.

One interesting, and somewhat curious finding in this study -as well as Alcohol Study 1- was that treatment tests coinciding with rising, peak, and falling BACs revealed a similar degree of impairment in inhibitory control and response flexibility. The failure to observe greater impairment at peak BACs of 73 dL/kg differs from evidence obtained from motor skills tasks. Motor skill performance under a dose of alcohol comparable to that used in this thesis typically shows greatest impairment at the peak BAC, and some recovery as BACs begin to decline.

Alcohol Study 2 also explored the possibility that the most pronounced effects of alcohol on inhibitory control might be at the stop-signal delays closest in time to the go-signal on low-load tasks. This prediction received only modest support in the present study, although the greatest decline in inhibitory control under alcohol was again observed at the earliest stop-signal delay on the low-load task. As discussed in Alcohol Study 1, this result would not be predicted by "myopia" theories of inhibitory control.

In summary, the results of Alcohol Study 2 supported the hypotheses that a moderate dose of alcohol disrupts inhibitory control and response flexibility on cognitive tasks. The evidence further indicated that response flexibility under alcohol is adversely affected only following a failure to inhibit a first response.

DISCUSSION

This thesis developed go-stop and change tasks to measure the effects of a moderate dose of alcohol on inhibitory control and response flexibility when low or high information processing was required to respond to go-signals. It was shown that better inhibitory control was displayed drug-free and under alcohol when the go-stop and change tasks required more information processing. However, regardless of the information processing manipulation, alcohol impaired performance. The first study demonstrated that alcohol reduced inhibitory control, and the degree of impairment did not differ when the cognitive processing required to respond to a go-signal was increased. The second study replicated these findings and demonstrated that alcohol impaired response flexibility by slowing the time required to make a second response following a failure to inhibit a first response. Both studies also showed that alcohol impaired inhibitory control without affecting the reaction time to go-signals.

The results of the experiments were based on comparing the performance of social drinkers who received alcohol to those who expected alcohol but received a placebo. The groups did not differ on any measure of their drinking habits, or on their pretreatment performance on the go-stop and change tasks. Thus it appears reasonable to conclude that alcohol disrupted inhibitory control and response flexibility. An important implication of this conclusion is that a moderate dose of alcohol can selectively impair cognitive executive processes involved in response flexibility and inhibitory control.

Many theorists have postulated that alcohol affects behaviour by impairing the ability to extract and process information provided by cues in the environment. The thesis research investigated this possibility by manipulating the information processing demands of go-stop

and change tasks without altering any other parameters of the tasks. The information processing manipulation systematically influenced the reaction time to go-signals and the number of inhibitions displayed. However, the high or low information processing loads did not affect the intensity of alcohol-induced impairment in inhibitory control and response flexibility on the go-stop tasks and the change tasks. To test the effect of manipulating information processing, all other parameters of the go-stop and change tasks had to be held constant. This requirement constrained the degree to which the low and high information load of go-signals could differ (see discussion in Appendix A). It might be argued that the information processing manipulation was too slight to affect the intensity of alcohol impairment on inhibitory control and response flexibility. However, the evidence is still inconsistent with broad proposal that alcohol-induced impairment increases as cues for a response require more information processing (e.g., Maylor & Rabbitt, 1987; Steele & Southwick, 1985).

The demonstration that a moderate dose of alcohol impairs response flexibility when inhibition fails might have important implications for understanding the effect of alcohol on behavioural control. Individuals with damage to the frontal cortices often display a fairly general response perseveration which is demonstrated as a deficit in switching to an alternative response. If alcohol reduces response flexibility by causing a generalized response perseveration, then flexibility -measured by the reaction time of a second response- should have been slower after both inhibitions and failures to inhibit. Because alcohol only impaired response flexibility when inhibition failed, it appears that a mild dose of alcohol does not result in a generalized perseveration of responding.

The specific impairing effect of alcohol on response flexibility when inhibition fails is a new finding. Some reasons that alcohol might specifically compromise response flexibility following failures to inhibit can be suggested. Following Logan and Burkell (1986), it could be argued that when inhibition fails, the completion of the first response competes with the initiation and completion of a second response. Thus, a moderate dose of alcohol might increase the time required to resolve this response conflict, thereby delaying the completion of the second response. On the other hand, Norman and Shallice (1986) argued that in competitive response situations -such as go-stop and change tasks-, an intact executive system functions to detect and correct errors. The finding that alcohol reduces inhibitory control indicates that alcohol disrupts one aspect of the executive system. If alcohol also impairs the ability to detect and correct errors, then it might take longer for an intoxicated individual to detect a failure to inhibit, and this might slow the reengagement of a second response.

Although the information processing manipulation used in this thesis did not interact with the overall degree of inhibitory control displayed under alcohol, it did interact with the pattern of inhibitory control displayed at the stop-signal delays under alcohol. Evidence from the low-load go-stop task in Alcohol Study 1 indicated that the greatest reduction in inhibitory control in the alcohol group was observed at the shorter stop-signal delays. This effect on the low-load change task was partially replicated in Alcohol Study 2, where the greatest reduction in inhibitory control was observed when the go-signal and stop-signal were presented simultaneously. These findings are not consistent with the general notion that greater alcohol-induced impairment should be observed when the processing required to respond on a task is increased (e.g., Maylor & Rabbitt, 1987). According to this notion, greater impairment should

be displayed with longer stop-signal delays on tasks, because they necessitate a greater degree of executive control. However, on both go-stop and change tasks, greater impairment under alcohol tended to coincide with the shorter stop-signals, and this tendency was most evident on the simpler, low information processing tasks. It appears that when go-signals require little information processing, a moderate dose of alcohol interferes with the ability to process competing signals that are presented closer together in time.

The ability to process targets that are presented simultaneously or in rapid succession is thought to depend on intact executive cognitive processing (Posner & DiGirolamo, in press). Recent neuroimaging work has noted increased activity in the anterior cingulate region on tasks when more than one target stimulus must be processed at a time (Raichle et al., 1994). Thus, if alcohol disturbs functions associated with frontal areas, such as the anterior cingulate, then the ability to process synchronous information might be impaired. The disruption of this process might explain why alcohol impaired inhibitory control to a greater degree when stop-signals occurred in closer proximity to low-load go-signals.

The experiments in this thesis scheduled three treatment tests of performance to coincide with rising, peak, and falling blood alcohol concentrations (BACs). However, the impairment of inhibitory control and response flexibility did not vary as a function of these changes in BAC. These findings are inconsistent with evidence from psychomotor skill tasks, where doses of alcohol comparable to those used in this thesis induce impairment that intensifies as BAC increases, and decreases as BAC declines (e.g., Vogel-Sprott, 1992; Easdon & Vogel-Sprott, 1996b). The reason for the sensitivity to changing BACs of psychomotor tasks and the comparative insensitivity of cognitive tasks is perplexing. It might

be due to the minimal motor component required in the go-stop and change tasks. These tasks required no complex muscle movements: subjects simply rested their fingers on the response keys and only had to press a key to register their response. Recent evidence from functional neuroimaging has noted that a moderate dose of alcohol reduces glucose metabolism in the frontal cortex and cerebellum (de Wit et al., 1990). This suggests that alcohol might interfere with the coordination of skilled motor movements, as well as cognitive processing. Thus, it could be argued that the alcohol-induced impairment observed on psychomotor tasks has both a cognitive and a motor component. The sensitivity to BAC under a moderate dose of alcohol observed on psychomotor tasks might result because the motor component of the behaviour is more sensitive to changing BACs than is the cognitive component. Conversely, on tasks without a complex motor component, the cognitive impairment might be relatively invariant within a moderate range of BACs. This might account for the stable level of alcohol-induced impairment displayed on the cognitive go-stop and change tasks. This hypothesis could be tested by manipulating the complexity of the motor response required on go-stop and change tasks. If the sensitivity to BACs observed on psychomotor tasks depends on the motor response demands of the tasks, then this sensitivity should also be observed on go-stop and change tasks when greater motor skill is required to make a response.

The experiments presented in this thesis are the first to use go-stop and change paradigms with different information processing demands to investigate the effects of a moderate dose of alcohol on behavioural measures of inhibitory control and response flexibility. The dose of alcohol is consistent with that typically consumed by social drinkers. Moderate doses of alcohol have been found to impair performance on a number of cognitive

tasks (e.g., Holloway, 1995), and this research was designed to determine whether such a dose impairs cognitive processing governing inhibitory control and response flexibility. Previous studies (e.g., Shillito, King, & Cameron, 1974) have noted that doses of alcohol equivalent to those used in the present studies have little effect on simple and choice reaction time measures. However, simple reaction time measures start to be affected at BACs above 100mg/dL (e.g., Maylor, Rabbitt, James, & Kerr, 1992). This finding suggests that alcohol might impair inhibitory control and response flexibility without affecting reaction time only at moderate BACs. Not all tasks and cognitive processes require the same degree of executive control or supervisory attention (Norman & Shallice, 1986), and the evidence in this thesis indicates that executive cognitive processes (i.e., inhibitory control and response flexibility) are compromised at BACs that do not affect more basic processes (i.e., reaction time to the go-signal) that require less executive control. However, the effects of higher doses of alcohol on performance of the go-stop and change tasks remain to be tested.

The degree to which inhibitory control and response flexibility were impaired by alcohol in this thesis did not interact with information processing that altered the amount of visual search required to complete a go-response. Future studies could employ other approaches to increase the information processing demands of the tasks, such as making the detection of the target stimulus contingent on the presence of conjoined features (a la Treisman & Gelade, 1980). Different methods of increasing the processing demands of the tasks might help to clarify whether alcohol-induced impairment is affected by other types of information processing demands.

Previous investigations of the effects of alcohol on information processing and

behavioural control have used indirect measures -such as questionnaires, neuropsychological tasks, and competitive laboratory paradigms- to evaluate the effects of the drug. Studying the effects of alcohol on information processing and behavioural control with sensitive cognitive measures of inhibitory control and response flexibility is an important advance in this respect. The go-stop tasks used in this thesis provided direct behavioural measures of the degree to which a moderate dose of alcohol impairs the ability to inhibit an ongoing response. Similarly, the change tasks used in this thesis gave direct evidence that a moderate dose of alcohol delays the display of a second response following a failure to inhibit a first response.

It has been argued that behaviour observed under alcohol tends to conform to learned social norms of conduct based on the consequences of the behaviour under the drug (e.g., MacAndrew & Edgerton, 1969). The present studies did not present subjects with any norms for performance under alcohol or any feedback or consequences of behaviour. This is an important consideration because these factors have typically confounded results in studies of alcohol effects on social behaviours. Thus, an important contribution of this thesis is that it demonstrates that in the absence of any standards of behaviour, inhibitory control and response flexibility are impaired under alcohol. Moreover, an advantage of the present approach is that future studies could introduce feedback and consequences related to task performance in a systematic fashion to examine their effects on inhibitory control and response flexibility.

The go-stop and change tasks developed in this thesis might be useful to study the effects of other drugs on inhibitory control and response flexibility. For example, the sedative actions of the benzodiazepines are thought to result from these drugs amplifying the effects of

the inhibitory neurotransmitters adenosine and GABA (McKim, 1991). By testing performance on go-stop and change tasks under the influence of benzodiazepines, it might be possible to trace the neurotransmitter systems associated with sedatives that are involved in inhibitory control and response flexibility. Thus, pharmacological tools and cognitive tasks could be used to build neurophysiological models of cognitive flexibility.

The development of the go-stop and change tasks used in this thesis was guided by the race model of inhibitory control (Logan & Cowan, 1984). The tasks were tailored to address specific questions about the effects of alcohol, and their adequacy was tested under drug-free conditions prior to their use in the alcohol studies. Drug-free testing verified some assumptions of the race model of inhibitory control. As predicted, when the go-signal required more cognitive processing, the go-response was slowed and more inhibitions were displayed. Drug-free tests (Appendix B) also provided support for the prediction that the go-process and the stop-process are independent. Further testing (Appendix D) comparing the performance on go-stop and change tasks with different cognitive loads confirmed that slowing the go-response led to more inhibitions on both go-stop and change tasks. In addition, reaction time to the go-signal was slightly slower on change tasks than on go-stop tasks, suggesting that requiring a second response placed additional demands on cognitive processing.

Other researchers have found deficits in cognitive flexibility in children diagnosed with ADHD that bear some resemblance to the effects of alcohol observed in this thesis. However, it is important to consider that these similarities in performance do not necessarily imply that the nature of the impairment is the same in both groups. Studies that have used go-

stop and change paradigms to study the performance of individuals with ADHD have found that inhibitory control, response flexibility, and reaction time to the go-signal were impaired (e.g., Schachar, Tannock, Marriot, & Logan, 1995). Thus, there is apparently no selective impairment of inhibitory control and response flexibility in ADHD children. The variability in measures of performance of children with ADHD is typically quite high, and these children tend to "miss" (or simply do not respond) to many go-signals. None of these aspects of performance characterized the undergraduate sample used in this thesis. However, the findings do suggest the importance of considering other factors that might be involved in the measurement of cognitive flexibility, such as the ability to direct attention to a task. In addition, the differences in task performance in different populations raise the possibility that cognitive flexibility might not depend on a single process.

Implications for neuropsychological assessment and research

The adoption of paradigms developed in cognitive science to study drug effects represents an important advance in measuring the effects of drugs on cognitive processes. The investigation of the effects of a moderate dose of alcohol on the cognitive processes of a neurologically intact population requires tasks that are reliable and sensitive. Standard neuropsychological instruments were developed primarily to localize lesions in populations who had sustained some sort of brain injury. Consequently, these instruments often lack the sensitivity to detect mild deficits in cognitive processing in a neurologically intact population (Bates & Tracy, 1990). For example, the Wisconsin Card Sort Task (WCST) has been used extensively as a measure of executive control, and numerous investigations in neuropsychology have reported the sensitivity of the WCST to frontal damage (Fuster, 1997).

However, the WCST has a number of limitations that restrict its applicability in drug research. As is the case for many neuropsychological tests, the WCST can only be administered a limited number of times because an individual will usually learn the appropriate pattern of responding after the test has been completed once. Thus many neuropsychological instruments are ill-suited to investigations of change in cognitive processing following an acute dose of alcohol. More generally, standard neuropsychological instruments provide a rich amount of information by tapping a number of cognitive processes simultaneously, but this makes it difficult to identify changes in specific cognitive functions that might be attributable to a drug.

Much neuropsychological evidence has pointed to the frontal cortices as the seat of executive functioning. Although it would be difficult to dismiss the contribution of these areas to executive cognitive control, it is equally important to avoid localising executive processes exclusively to the frontal areas. Extensive neuroanatomical evidence indicates the complexity of the afferent and efferent connections of the frontal lobe with other brain areas (e.g., Pandya & Barnes, 1987). Thus, it is likely that altering any component or connection in this extensive network will affect other components of the system, and will have repercussions for the cognitive processing and behavioural output associated with the system.

Most current investigations of cognitive processes employing functional neuroimaging use a subtractive method to identify brain regions active during task performance. This method typically involves scanning an individual at rest, or while performing a task that excludes the process of interest, and again while the person is engaged in a task that putatively taps the process of interest. The activation associated with the resting scan is then subtracted

from the activation of the test scan, and the remaining areas of activation are interpreted as important to the process of interest. A drawback to this approach is that it tends to overlook the functional interrelations between brain areas and implies a localisation of functions.

An alternative to the subtractive method of analysing neuroimaging data is to focus on how the activation of different areas covary during testing. A covariance approach has the advantage of being more compatible with the complex interconnectedness of the nervous system. This approach assumes that the nervous system is a series of interconnected parallel networks, rather than a collection of specialized areas (McIntosh & Gonzalez-Lima, 1994). Using a combination of functional neuroimaging techniques and multivariate analysis, it might be possible to identify patterns of neural activity between those areas that are characteristic of a given executive process. This research approach could potentially dissociate executive cognitive functions, such as behavioural sequencing, planning, and shifting response sets, based on the underlying neural interactions from which they emerge. Such an approach might also aid in determining whether the disruptions in behavioural control observed in different populations (e.g., ADHD children, social drinkers under alcohol, the elderly) can be attributed to common or different networks of neural activation.

A recurring criticism of neuroscience investigations of the effects of alcohol is that it has been difficult to link changes in neuronal functioning with changes in behaviour (e.g., Hunt, 1993). However, by combining the tasks developed in this thesis with a network approach to analysing neuroimaging data, it might be possible to clarify the neurophysiological mechanisms underlying the effects of alcohol on inhibitory control and response flexibility. Thus, the combination of these techniques could potentially offer some

insight into how alcohol-induced changes in neurophysiology might affect behaviour.

Conclusions

Research from a number of disciplines has noted that alcohol consumption is associated with impaired behavioural control. This thesis used task paradigms developed in cognitive science to directly measure behavioural inhibition and response flexibility. Results indicated that a moderate dose of alcohol selectively impairs inhibitory control and response flexibility without affecting the reaction time to a go-signal. The tasks used in this thesis manipulated the information processing required to respond to a go-signal and showed that better inhibitory control was displayed drug-free and under alcohol when the go-signals required higher information processing. However, the degree to which alcohol impaired inhibitory control and response flexibility was similar under both information processing conditions. The tasks developed and used in this thesis represent an innovative approach to the investigation of the effects of alcohol on cognitive control of behaviour in two respects: they provide direct behavioural measures of changes in cognitive control and they provide an experimental procedure that can introduce and test the effect of environmental consequences of behaviour on cognitive control. In addition, the procedures developed in this thesis in combination with functional neuroimaging techniques might also help to identify the neural networks associated with behavioural control, and might clarify how alcohol acts upon these networks to affect behavioural control.

REFERENCES

Adams, K.M., Gilman, S., Koeppe, R.A., et al. (1993). Neuropsychological deficits are correlated with frontal hypometabolism in PET studies of older alcoholic patients. *Alcoholism: Clinical and Experimental Research, 17,* 205-210.

Arbuthnott, K.D. (1995). Inhibitory mechanisms in cognition: Phenomenon and models. *Current Psychology of Cognition, 14,* 3-45.

Bates, M.E. (1989). The effect of repeated occasions of alcohol intoxication on two processes involved in the visual discrimination of movement. *Journal of Studies on Alcohol, 50,* 143-154.

Bates, M.E., & Tracy, J.I. (1990). Cognitive function in young social drinkers: Is there impairment to detect? *Journal of Abnormal Psychology, 99,* 424-249.

Bushman, B.J., & Cooper, H.M. (1990). Effects of alcohol on human aggression: An integrative research review. *Psychology Bulletin, 107,* 341-354.

Carpenter, J.A. (1962). Effects of alcohol on some psychological processes. *Quarterly Journal of Studies on Alcohol, 23,* 274-314.

Cherek, D.R., Steinberg, J.L., & Manno, B.R. (1985). Effects of alcohol on human aggressive behavior. *Journal of Studies on Alcohol, 46,* 321-328.

Cherek, D.R., Spiaga, R., Steinberg, J.L., & Kelly, T.H. (1990). Human aggressive responses maintained by avoidance or escape from point loss. *Journal of the Experimental Analysis of Behavior, 53,* 293-303.

Chipperfield, B., & Vogel-Sprott, M. (1984). Student's drinking habits and family history of social drinking. *Canadian Psychology, 25,* 2a.

Collins English Dictionary. (1979). Glasgow: William Collins Sons and Company Ltd.

Damasio, A.R., & Anderson, S.W. (1993). The frontal lobes. In K.M. Heilman and E. Valenstein (eds.), *Clinical Neuropsychology, 3rd ed.* (pp. 409-460). New York: Oxford University Press.

Damasio, A.R., Tranel, D., & Damasio, H. (1990). Individuals with sociopathic behavior caused by frontal damage fail to respond automatically to social stimuli. *Behavioural Brain Research, 41,* 81-94.

de Wit, H., Metz, J., Wagner, N., et al. (1990). Behavioral and subjective effects of ethanol: relationship to cerebral metabolism using PET. *Alcoholism, 14,* 482-489.

Easdon, C.M., & Vogel-Sprott, M. (1996a). Assessing acute effects of alcohol by neuropsychological tests. *Alcoholism: Clinical and Experimental Research, 20,* 77A.

Easdon, C.M., & Vogel-Sprott, M. (1996b). Drug-free behavioral history affects social drinkers' tolerance to a challenge dose of alcohol. *Journal of Studies on Alcohol, 57,* 591-597.

Easdon, C.M., & Vogel-Sprott, M. (1996c). The effect of alcohol on inhibitory control: a test of the "race" model. *Proceedings of the Sixth annual meeting of the Society for Brain, Behaviour and Cognitive science,* 38.

Fenwick, P.B.C., Ioannides, A.A., Fenton, G.W., et al. (1993). Estimates of brain activity using magnetic field tomography in a GO/NOGO avoidance paradigm. *Brain Topography, 5,* 275-282.

Feutchwanger, E. (1923). Die funktionen des stirnhirns: Ihre pathologie und psychologie. Monogr. Gesamtgeb. Neurol. Psychiatr. (Berlin), 38, 4-194. (from J.M. Fuster, 1997,

The Prefontal Cortex, 3rd ed. New York: Raven Press).

Fillmore, M.T., & Vogel-Sprott, M. (1995). Expectancies about alcohol-induced motor impairment predict individual differences in responses to alcohol and placebo. *Journal of Studies on Alcohol, 56,* 90-98.

Frith, C.D., Friston, K., Liddle, P.E., & Frackowiak, R.S.J. (1991). Willed action and the prefrontal cortex in man: a study with PET. *Proceedings of the Royal Society, 244,* 241-246.

Fuster, J.M. (1997). *The Prefrontal Cortex, 3rd ed.* New York: Raven Press.

Gesa, G.L., Muntoni, F., Vargui, L., & Mereu, G. (1985). Low doses of ethanol activate dopaminergic neurons in the ventral tegmental area. *Brain Research, 348,* 201-203.

Hawkins, J.M., & Allen, R. (eds.). (1991). *The Oxford Encyclopedic English Dictionary.* New York: Oxford University Press.

Holloway, F.A. (1995). Low-dose alcohol effects on human behavior and performance. *Alcohol, Drugs and Driving, 11,* 39-56.

Hunt, W.A. (1993). Neuroscience research: How has it contributed to our understanding of alcohol abuse and alcoholism? A Review. *Alcoholism: Clinical and Experimental Research, 17,* 1055-1065.

Imperato, A., & Di Chiara, G. (1986). Preferential stimulation of dopamine release in the nucleus accumbens of freely moving rats by ethanol. *Journal of Pharmacology and Expeimental Therapeutics, 239,* 219-228.

Ingvar, D.H. (1985). "Memory of the future": an essay on the temporal organization of conscious awareness. *Human Neurobiology, 4,* 127-136.

Ingvar, D.H. (1996). The will of the brain: cerebral correlates of willful acts. In A.R. Damasio, H. Damasio, and Y. Christen, (eds.), *Neurobiology of Decision-Making.* (pp. 115-123). New York: Springer-Verlag.

Ito, T.A., Miller, N., & Pollock, V.E. (1996). Alcohol and aggression: A meta-analysis on the moderating effects of inhibitory cues, triggering events, and self-focused attention. *Psychological Bulletin, 120,* 60-82.

Jones, B.M. (1974). Circadian variation in the effects of alcohol on cognitive performance. *Quarterly Journal of Studies on Alcohol, 35,* 1212-1219.

Jonides, J., Smith, E.E., Koeppe, R.A., Awh, E., Minoshima, S., & Mintun, M.A. (1993). Spatial working memory in humans as revealed by PET. *Nature, 363,* 623-625.

Kahneman, D. (1973). *Attention and Effort.* N.J.: Prentice Hall.

Kolb, B. & Whishaw, I.Q. (1996). *Fundamentals of Human Neuropsychology, 4th ed.* New York: W.H. Freeman and Company.

Kok, A. (1986). Effects of degradation of visual stimulation components of event-related potential (ERP) in Go/Nogo reaction tasks. *Biological Psychology,* 23, 21-38.

Korytnyk, N.X., & Perkins, D.V. (1983). Effects of alcohol versus expectancy of alcohol on the incidence of graffiti following an experimental task. *Journal of Abnormal Psychology, 92,* 382-385.

Leslie, S.W., Barr, E., Chandler, J., & Farrar, R.P. (1983). Inhibition of fast- and slow-phase depolarization-dependent synaptosomal calcium uptake by ethanol. *Journal of Pharmacology and Experimental Therapeutics, 225,* 571-575.

Lezak, M.D. (1983). *Neuropsychological Assessment, 2nd ed.* New York: Oxford University

Press.

Logan, G.D. (1994). On the ability to inhibit thought and action: A users' guide to the stop-signal paradigm. In D. Dagenbach and T.H. Carr (eds.), *Inhibitory Processes in Attention, Memory, and Language* (pp. 189-239). Toronto: Academic Press.

Logan, G.D., & Burkell, J. (1986). Dependence and independence in responding to double stimulation: A comparison of stop, change, and dual-task paradigms. *Journal of Experimental Psychology: Human Perception and Performance, 12,* 549-563.

Logan, G.D., & Cowan, W.B. (1984). On the ability to inhibit thought and action: A theory of an act of control. *Psychological Review, 91,* 295-327.

Lovinger, D.M., White, G., & Weight, F.F. (1989). Ethanol inhibits NMDA-activated ion current in hippocampal neurons. *Science, 243,* 1721-1724.

Luce, R.D. (1986). *Response times: their role in inferring elementary mental organization.* Oxford: Claredon Press.

Luria, A.R. (1980). *Higher Cortical Functions in Man, 2nd ed.* New York: Basic Books, Inc..

MacAndrew, C., & Edgerton, R. (1969). *Drunken comportment: A social explanation.* Chicago: Aldine.

MacDonald, T.K., Zanna, M.P., & Fong, G.T. (1995). Decision making in altered states: Effects of alcohol on attitudes toward drinking and driving. *Journal of Personality and Social Psychology, 68,* 973-985.

Malloy, P., Bihrle, A., Duffy, J., & Cimino, C. (1993). The orbitomedial frontal syndrome. *Archives of Clinical Neuropsychology, 8,* 185-201.

Malloy, P., Rasmussen, S., Braden, W., & Haier, R.J. (1989). Topographic evoked potential mapping in obsessive compulsive disorder: Evidence of frontal lobe dysfunction. *Psychiatry Research, 28,* 63-71.

Maylor, E.A. & Rabbitt, P.M. (1987). Effects of alcohol and practice on choice reaction time. *Perception and Psychophysics, 42,* 465-475.

Maylor, E.A., Rabbitt, P.M., James, G.H., & Kerr, S.A. (1992). Effects of alcohol, practice, and task complexity on reaction time distributions. *Quarterly Journal of Experimental Psychology: Human Experimental Psychology, 49A,* 119-139.

McIntosh, A.R., & Gonzalez-Lima, F. (1994). Structural equation modeling and its application to network analysis in functional brain imaging. *Human Brain Mapping, 2,* 2-22.

McKim, W.A. (1991). *Drugs and behavior: An introduction to behavioral pharmacology, 2nd ed.* New Jersey: Prentice Hall.

Mitchell, M.C. (1985). Alcohol-induced impairment of central nervous system function: Behavioral skills involved in driving. *Journal of Studies on Alcohol, supplement 10,* 109-116.

Moskowitz, H. (1973). Laboratory studies on the effects of alcohol on some variables related to driving. *Journal of Safety Research, 5,* 185-199.

Mulvihill, L.E., Skilling, T.A., & Vogel-Sprott, M. (1997). Alcohol and the ability to inhibit behavior in men and women. *Journal of Studies on Alcohol, 58,* 600-605.

Murdoch, D., Pihl, R.O., & Ross, D. (1990). Alcohol and crimes of violence: Present issues. *International Journal of Addictions, 25,* 1065-1081.

Newlin, D.B., Golden, C.J., Quaife, M., et al. (1982). Effect of alcohol ingestion on regional cerebral blood flow. *International Journal of Neuroscience, 17,* 145-150.

NIAAA Research Monograph no. 24. (1992). *Alcohol and Interpersonal Violence,* S.E. Martin (ed.). U.S. Department of Health and Human Services.

Norman, D.A., & Shallice, T. (1986). Attention to action: Willed and automatic control of behavior. In R.J. Davidson, G.E. Schwartz, and D. Shapiro (eds.), *Consciousness and Self-Regulation* (pp. 1-18). New York: Plenum Press.

Pandya, D.N., & Barnes, C.L. (1987). Architecture and connections of the frontal lobe. In E. Perecman (ed.), *The Frontal Lobes Revisited* (pp. 41-72). New York: IRBN Press.

Pernanen, K. (1976). Alcohol and crimes of violence. In B. Kissin and H. Begleiter (eds.), *The Biology of Alcoholism: Vol. 4. Social aspects of alcoholism* (pp. 351-444). New York: Plennum.

Peterson, J.B., Rothfleisch, J., Zelazo, P.D., & Pihl, R.O. (1990). Acute alcohol intoxication and cognitive functioning. *Journal of Studies on Alcohol, 51,* 114-122.

Petrides, M., & Milner, B. (1982). Deficits on subject-ordered tasks after frontal- and temporal-lobe lesions in man. *Neuropsychologia, 20,* 249-262.

Pihl, R.O., & Peterson, J.B. (1991). A biobehavioural model for the inherited predisposition to alcoholism. *Alcohol and Alcoholism, Supplement 1,* 151-156.

Pihl, R.O., Zeichner, A., Niaura, R., Nagy, K., & Zacchia, C. (1981). Attribution and alcohol-mediated aggression. *Journal of Abnormal Psychology, 90,* 468-475.

Posner, M.I. (1978). *Chronometric Explorations of the Mind.* New York: Wiley.

Posner, M.I. & DiGirolamo, G.J. (in press). Conflict, target detection and cognitive control.

In R. Parasuraman (ed.), *The Attentive Brain.* Cambridge: MIT Press.

Raichle, M.E., Fiez, J.A., Videen, T.O., et al. (1994). Practice-related changes in human brain functional anatomy during nonmotor learning. *Cerebral Cortex, 4,* 8-26.

Riegler, G.L. (1986). Are stop and go processes independent in the stop-signal paradigm? Unpublished master's thesis, Purdue University, West Lafayette, IN. (from G.D. Logan, 1994, On the ability to inhibit thought and action: A users' guide to the stop-signal paradigm. In D. Dagenbach and T.H. Carr (eds.), *Inhibitory Processes in Attention, Memory, and Language* (pp. 189-239). Toronto: Academic Press).

Robbins, T.W. (1996). Dissociating executive functions of the prefrontal cortex. *Philosophical Transactions of the Research Society of London B, 351,* 1463-1471.

Rohsenow, D.J., & Bachorowski, J.A. (1984). Effects of alcohol and expectancies on verbal aggression in men and women. *Journal of Abnormal Psychology,* 93, 418-432.

Schachar, R., Tannock, R., & Logan, G.D. (1993). Inhibitory control, impulsiveness, and attention deficit hyperactivity disorder. *Clinical Psychology Review, 13,* 721-739.

Schachar, R., Tannock, R., Marriot, M., & Logan, G.D. (1995). Deficient inhibitory control in attention deficit hyperactivity disorder. *Journal of Abnormal Child Psychology, 23,* 411-437.

Schwartz, J.A., Speed, N.M., Gross, M.D. et al. (1993). Acute effects of alcohol administration on regional cerebral blood flow: the role of acetate. *Alcoholism: Clinical and Experimental Research, 17,* 1119-1123.

Shallice, T. (1982). Specific impairments of planning. *Philosophical Transactions of the Research Society of London B, 298,* 199-209.

Shallice, T., & Burgess, P. (1991). Higher-order cognitive impairments and frontal lobe lesions in man. In H.S. Levin, H.M. Eisenberg, and A.L. Benton (eds.), *Frontal Lobe Function and Dysfunction.* (pp. 125-138). New York: Oxford University Press.

Shallice, T., & Burgess, P. (1993). Supervisory control of action and thought selection. In A. Baddeley and L. Weiskrantz (eds.), *Attention: Selection, awareness and control.* (pp. 171-187). Oxford: Clarendon Press.

Shillito, L.M., King, E.L., & Cameron, C. (1974). Effects of alcohol on choice reaction time. *Quarterly Journal of Studies on Alcohol, 35,* 1023-1034.

Steele, C.M., & Josephs, R.A. (1990). Alcohol myopia: Its prized and dangerous effects. *American Psychologist, 45,* 921-933.

Steele, C.M., & Southwick, L. (1985). Alcohol and social behavior I: The psychology of drunken excess. *Journal of Personality and Social Psychology, 48,* 18-34.

Sternberg, S. (1969). The discovery of processing stages: Extensions of Donder's method. In W.G. Koster (ed.), *Attention and Performance II, Acta Psychologica, 30,* 276-315.

Tannock, R., Schachar, R., & Logan, G.D. (1995). Methylphenidate and cognitive flexibility: Dissociated dose effects in hyperactive children. *Journal of Abnormal Child Psychology, 23,* 235-266.

Tarter, R.E., Jones, B.M., Simpson, C.D., & Vega, A. (1971). Effects of task complexity and practice on performance during acute alcohol intoxication. *Perceptual and Motor Skills, 33,* 307-318.

Treisman, A., & Gelade, G. (1980). A feature integration theory of attention. *Cognitive Psychology, 12,* 97-136.

Vogel-Sprott, M. (1992). *Alcohol Tolerance and Social Drinking: Learning the Consequences.* New York: The Guilford Press.

Volkow, N.D., Mullani, N., Gould, L., et al. (1988). Effects of acute alcohol intoxication on cerebral blood flow measured with PET. *Psychiatry Research, 24,* 201-209.

Wise, R.A., & Bozarth, M.A. (1987). A psychomotor stimulant theory of addiction. *Psychological Review, 94,* 469-492.

Zeichner, A., & Pihl, R.O. (1979). Effects of alcohol and behavior contingencies on human aggression. *Journal of Abnormal Psychology, 88,* 153-160.

Zeichner, A., & Pihl, R.O. (1980). The effects of alcohol and instigator intent on human aggression. *Journal of Studies on Alcohol, 41,* 265-276.

APPENDICES

Appendix A

Development of go-stop tasks

Slowing the go-response has clear implications for the degree of inhibitory control displayed on a go-stop task. If the response to the go-signal is slowed and the stop-process is held constant, it follows that -in the parlance of the race model- the stop-process should win the race more often, resulting in fewer failures to inhibit and a greater display of inhibitory control.

A test of this hypothesis requires two go-stop tasks that differ only in the time required to respond to the go-signal. Although the response time to the go-signal might be manipulated by varying the information processing requirements of a go-signal, there were no reports of such tasks in the literature. Thus, to test the effect of alcohol on inhibitory control on such tasks, it was first necessary to develop and validate them under drug-free conditions. This was the goal of the present study.

Manipulating the go-signal

Evidence from the cognitive literature indicates that slowing the go-response could be accomplished in a number of ways. A common manipulation that results in more cognitive processing, and a consequent slowing of a go-response to a target stimulus, is to increase the search necessary to detect a target. Treisman and Gelade (1980) made target detection contingent on the presence of a conjunction of features and noted that as the display size was increased, reaction times to detect the target also increased. Posner (1978) reported that response times could be slowed by increasing the size of the target set. Another method that

slows response time is to increase the visual search required to identify the target (Sternberg, 1969). These three manipulations of target detection admittedly require different types and degrees of information processing (for a thorough discussion, see Luce, 1986), and entire literatures have been devoted to exploring their implications for attentional capacity and information processing. However, keeping in mind the purpose of this study, they all have the net effect of slowing the reaction time to a go-signal target.

An important consideration in modifying a go-stop task is that the complication of the go-signal should not be so extreme as to eliminate the observation of unsuccessful attempts to inhibit a response. In other words, an extremely complicated go-signal could slow the go-response to such an extent that the stop-process would always finish before the go-process, and subjects would always inhibit their response. In this case, there could be no meaningful measure of inhibitory control. Thus, it was necessary to create a go-stop task that slowed the completion of the go-response, yet still allowed for failures of inhibitory control.

Preliminary testing indicated that the requirements for go-signal manipulation were satisfied most parsimoniously by increasing the visual search required for target detection (Sternberg, 1969). Sternberg (1969) noted that for each additional distracter letter presented in a display, the reaction-time to a target go-signal (RTGO) would be slowed by approximately 10-15 ms. For example, a choice reaction-time task that presents one target letter and five distracter letters simultaneously, should require an RTGO that is approximately 60 ms longer than the RTGO when a target letter is presented in the absence of distracters.

These considerations guided the construction of two parallel go-stop tasks. One involving a low cognitive load presented a single go-signal, and the other requiring a higher

load presented the go-signal among an array of extraneous signals.

Establishing stop-signal delays

To ensure that a stop-signal cannot be anticipated, it should follow a go-signal infrequently and at different delay intervals. Thus, an additional goal of task development was to determine where the stop-signal delays should be placed following the onset of the go-signal in order to allow for the comparison of inhibitory control on both tasks. If the stop-signals were placed too close to the go-signal, it was reasoned that most individuals would be able to inhibit their response to the stop-signal most of the time on both tasks, resulting in a potential ceiling effect on inhibitions. Conversely, if the stop-signal delays were placed too far in time from the go-signal, so that most individuals could not inhibit a response on both tasks, this would create a floor effect. Thus, it was necessary to establish an appropriate range for the placement of the stop-signal delays that could maximise the information obtained from the tasks.

The appropriate placement of stop-signal delays can be achieved in a number of ways. Therefore, the choice of stop-signal delays is somewhat arbitrary (Logan, 1994). In the study of the effects of a moderate dose of alcohol on inhibitory control, Mulvihill et al. (1997) used a go-stop task that fixed stop-signal delays for all subjects at 50, 150, 250, and 350 ms following the onset of the go-signal. Using fixed stop-signal delays assumes that the stop-signals are placed in a range that will capture the inhibitory profile of most subjects. A potential drawback to this assumption is that individuals with faster response times to the go-signal will likely make fewer inhibitions than individuals with slower response times to the go-signal. One method of ensuring that individuals have the opportunity to make

approximately the same number of inhibitions on a go-stop task is to use a person's own performance to determine the stop-signal delays. This study evaluated the adequacy of setting stop-signal delays using an individual's task performance as a guide in developing two parallel go-stop tasks.

Method

Subjects

Subjects were nine right-handed male undergraduates recruited through their voluntary participation in the University of Waterloo Cognition and Perception "subject pool". Subjects received an honorarium of $7.00 for their participation.

Apparatus

Tasks. The performance of all subjects was measured on three go-stop tasks. All tasks were run using a 386/33 PC.

(1) Delay placement go-stop task (DP): This go-stop task helped establish a range of stop-signal delays for each subject that could be used in the other two go-stop tasks. This task estimated the stop-signal delay time at which an individual inhibited their responses to 50% of the stop-signals.

The task required subjects to discriminate between two letters (X and O), presented one at a time on a computer screen, by pressing one of two keys on a keyboard. The letters served as go-signals. Subjects were instructed to respond as quickly and as accurately as they could to the go-signals, and to try to withhold their response when the go-signal was followed by a stop-signal (a 900 Hz tone). One block of trials presented 128 go-signals, of which 32 were followed in a random order by a stop-signal. One block took 5 minutes and 34 seconds

to complete. A test consisted of three trial blocks, and each block was separated by a 30 second break.

To arrive at an estimate of the point where a stop-signal needed to be placed for a subject to inhibit a response 50% of the time, the computer adjusted the stop-signal delay by 20 ms after each stop-signal. If the response to the stop-signal was not inhibited, the next stop-signal was placed sooner after the onset of the go-signal; if the response to the stop-signal was inhibited, the next stop-signal was presented farther in time from the presentation of the go-signal.

A subject's mean 50% stop-signal delay time and the standard deviation (SD) of the subject's mean reaction time to the go-signal (RTGO) were used to determine the stop-signal delays for a subject on the subsequent go-stop tasks. As our goal was to place stop-signal delays at intervals following the onset of the go-signal that would elicit both inhibitions and failures to inhibit, we used a subject's 50% stop-signal delay time identified by the DP task, and the subject's mean (ms) reaction time and SD to identify four stop-signal delays. Two stop-signals delays were set earlier and two stop-signals later than the estimated 50% inhibition time. Stop-signal delays were set at -1.5, -.75, +.75, and +1.5 standard deviation (SD) units of the reaction time to the go-signal around a subject's 50% stop-signal delay time. These stop-signal delay times for each subject are shown in Table A1a. An example of the calculation of the stop-signal delays to be used in the subsequent go-stop tasks is provided using subject 1 in Table A1a. The DP task determined that the stop-signal delay had to be placed 124ms following the onset of the go-signal for subject 1 to inhibit 50% of the time. The subject's mean RTGO was 323ms with a SD of 46ms. Thus, the first stop-signal delay

Table A1a

Response reaction time, estimated 50% stop-signal delay, response accuracy, and stop-signal delays set for eight subjects on the DP task :

Subject	RTGO (ms) (SD)	estimated 50% delay (ms)	response accuracy (%)	delay -1.5 SD	delay -.75 SD	delay +.75 SD	delay +1.5 SD
1	323 (46)	124	92	55	89	159	194
2	346 (40)	166	93	106	136	196	227
3	456 (85)	199	97	71	135	263	327
4	387 (77)	181	99	66	123	239	290
5	500 (139)	251	99	42	147	356	460
7	446 (87)	217	98	87	152	282	348
8	357 (60)	89	98	5	44	134	178
9	345 (52)	164	91	87	125	203	241
sample	395 (73)	174 (51)	96 (3.3)	62 (33)	119 (36)	229 (72)	283 (94)

was placed at 124ms + (-1.5 X 46ms) = 55ms, the second stop-signal delay was placed at 124ms + (-.75 X 46ms) = 89ms, and so on. The stop-signal delay intervals calculated for each subject were then used when the individual performed the low- and high-load go-stop tasks.

(2) "Low-load" go-stop task (LGS): This computerised go-stop task was similar to the DP task in that a subject was required to discriminate between an "X" and "O" presented one at a time for 500 ms by pressing one of two keys on a keyboard. Each letter was preceded by a fixation point (.) for 500 ms. Each letter presentation constituted one trial and trials were separated by 2.5 seconds. One test consisted of four blocks of 88 go-signals, of which 24 were followed in a pseudo-random order by a stop-signal. Six stop signals were presented at each of the four delay intervals (i.e., at the -1.5, -.75, +.75, and +1.5 SD position in a subject's distribution of RTGO). The blocks were separated by a 30 second rest. Thus, a test presented 352 go-signals and 96 stop-signals, with 24 stop-signals at each of the four delays determined for a subject by the DP task. The number of inhibitions at each stop-signal delay and the total number of inhibitions made by a participant were recorded. This task also measured reaction time to the go signal when no stop-signal was present (RTGO), the mean reaction time when a subject failed to inhibit to a stop-signal (RTSTOP), and response accuracy (i.e., the number of times the subject pressed the correct key in response to a go-stimulus when no stop-signal was present).

(3) "High-load" go-stop task (HGS): This task was identical to the LGS task, except that the target letters (X and O) were presented along with five distracter letters (R, S, T, B, N) in a horizontal string in the centre of the computer screen. Either an "X" or an "O" was present in each six-letter string, and the subject had to identify these letters by pressing one of

two keys on the keyboard. All other specifications and measures recorded for this task were identical to the LGS task.

Procedure

Upon entering the laboratory, the subject read and signed an informed consent form (Appendix A1). The subject was then seated 60cm from a 14 inch 800 X 600 pixel computer monitor. After the DP task was explained, the subject had a 30 second practice period on the task and the experimenter then answered any questions the subject had about the task. When the subject understood the task instructions, the experimenter left the room and subjects performed a test on the DP task. The computer was programmed to present the trials and rests, and to record the subject's scores.

When the test on the DP task was completed, the subject entered a second room to relax while the experimenter collected the data from the DP task to determine the four stop-signal delay intervals to be used in the subsequent go-stop tasks. The subject then returned to the test room to perform the LGS task. The subject was told that the task was identical to the first task, except that the test would be a little longer. The experimenter left the room while the subject performed the test.

Following completion of the test on the LGS, subjects relaxed for five minutes before the experimenter provided the instructions for the HGS task. Subjects were informed that this task was identical to the one they had just completed, except that the "X" or the "O" would now be presented in a set of five other letters. Subjects were instructed to press the appropriate response key when they saw the "X" or the "O" among the string of letters and to try to withhold their response if they heard a tone. The experimenter then left the room while

the subject performed a test on the HGS task. Following the completion of the HGS task, the subject was debriefed and paid.

Results and Discussion

The data from the tests on each task are shown separately for subjects in Tables A1b (LGS), and A1c (HGS). One subject (#6) made many errors and appeared not to understand or follow task instructions. For these reasons, this subject was excluded from the experiment and all data analyses were performed with N=8.

Go-Response reaction time (RTGO). If the HGS task entails more information processing than the LGS task, then the RTGO and the reaction time to the go-signal when subjects failed to inhibit should be longer on the HGS than on the LGS task. A one-way repeated measures analysis of variance (ANOVA) of the mean reaction time to the go-signal (RTGO) on the two tasks obtained a significant effect of task ($F(1,7)=111.36$, $p<.0001$) (Table A2). In accord with the hypothesis, the mean RTGO (SD) on the HGS (410ms, SD=44) was significantly slower than the RTGO for the LGS (350ms, SD=40).

A 2 (task load) X 4 (stop-signal delay) repeated measures ANOVA of the reaction time to the go-signal when subjects failed to inhibit revealed a main effect of task load ($F(1,7)=21.68$, $p<.002$) (see Table A3), indicating that these responses were slower on the HGS (388ms, SD=63) than on LGS (334ms, SD=39). The absence of a significant main effect of stop-signal delay or interaction shows that the reaction time to the go-signal when inhibitions failed did not differ across stop-signal delays in either task.

A one-way repeated measures ANOVA tested the response accuracy on the LGS and HGS tasks. Although response accuracy was high on both tasks, the effect of task load

Table A1b

Performance measures for eight subjects on the LGS task:

subject	RTGO (ms)	RTSTOP (ms)	% response accuracy	proportion of inhibitions at delay -1.5 SD	proportion of inhibitions at delay -.75 SD	proportion of inhibitions at delay +.75 SD	proportion of inhibitions at delay +1.5 SD	total proportion of inhibitions
1	310	284	92	.67	.71	.21	.00	.40
2	322	322	93	.71	.75	.04	.04	.39
3	375	346	98	.79	.54	.17	.04	.39
4	337	331	96	.83	.63	.17	.00	.41
5	408	405	97	.67	.83	.00	.00	.38
7	406	369	96	.83	.79	.21	.04	.47
8	315	305	93	.88	.79	.08	.04	.45
9	330	309	93	.75	.58	.13	.00	.36
sample	350	334	95	.77	.70	.13	.02	.41

Table A1c

Performance measures for eight subjects on the HGS task:

subject	RTGO (ms)	RTSTOP (ms)	% response accuracy	proportion of inhibitions at delay -1.5 SD	proportion of inhibitions at delay -.75 SD	proportion of inhibitions at delay +.75 SD	proportion of inhibitions at delay +1.5 SD	total proportion of inhibitions
1	356	329	91	.79	.92	.46	.29	.61
2	392	348	95	.92	.83	.29	.21	.56
3	468	440	95	.96	.96	.46	.29	.67
4	388	331	89	.83	.63	.17	.00	.41
5	455	488	96	.92	.46	.00	.00	.34
7	461	455	95	.75	.75	.33	.08	.48
8	378	360	89	.79	.75	.38	.21	.53
9	380	349	92	.96	.79	.42	.08	.56
sample	410	388	93	.87	.76	.31	.15	.52

Table A2: Analysis of variance of the reaction time to the go-signal on the LGS and HGS tasks:

Source	SS	DF	MS	F	p
Task Load	14066.55	1	14066.55	111.36	.0001*
Error	884.19	7	126.31		

Table A3: Analysis of variance of the reaction time to the go-signal when subjects failed to inhibit at each stop-signal delay on the LGS and HGS tasks:

Source	SS	DF	MS	F	p
Task Load (T)	45776.74	1	45776.74	21.86	.002*
Error	14780.56	7	2111.51		
Delay (D)	5412.56	3	1804.19	1.40	.272
Error	27156.27	21	1293.16		
T X D	1413.93	3	471.31	.88	.469
Error	11297.94	21	538.00		

approached significance ($F(1,7)=4.90$, $p=.063$). This suggested that response accuracy was slightly lower on the HGS task (92.7%) than on the LGS task (94.8%). These levels of response accuracy are within the range of those typically observed on go-stop tasks (Logan, 1994).

In summary, the significantly longer response times to the complete the go-response on the HGS task suggest that it required more information processing than did completing the go-response on the LGS task.

Inhibitions. A 2 (task load) X 4 (stop-signal delay) repeated measures ANOVA of the number of inhibitions on each task is shown in Table A4. The results indicate a main effect of task load ($F(1,7)=8.04$, $p<.025$) and a main effect of stop-signal delay ($F(3,21)=290.98$,

Table A4: Analysis of variance of the number of inhibitions made at each stop-signal delay on the LGS and HGS tasks:

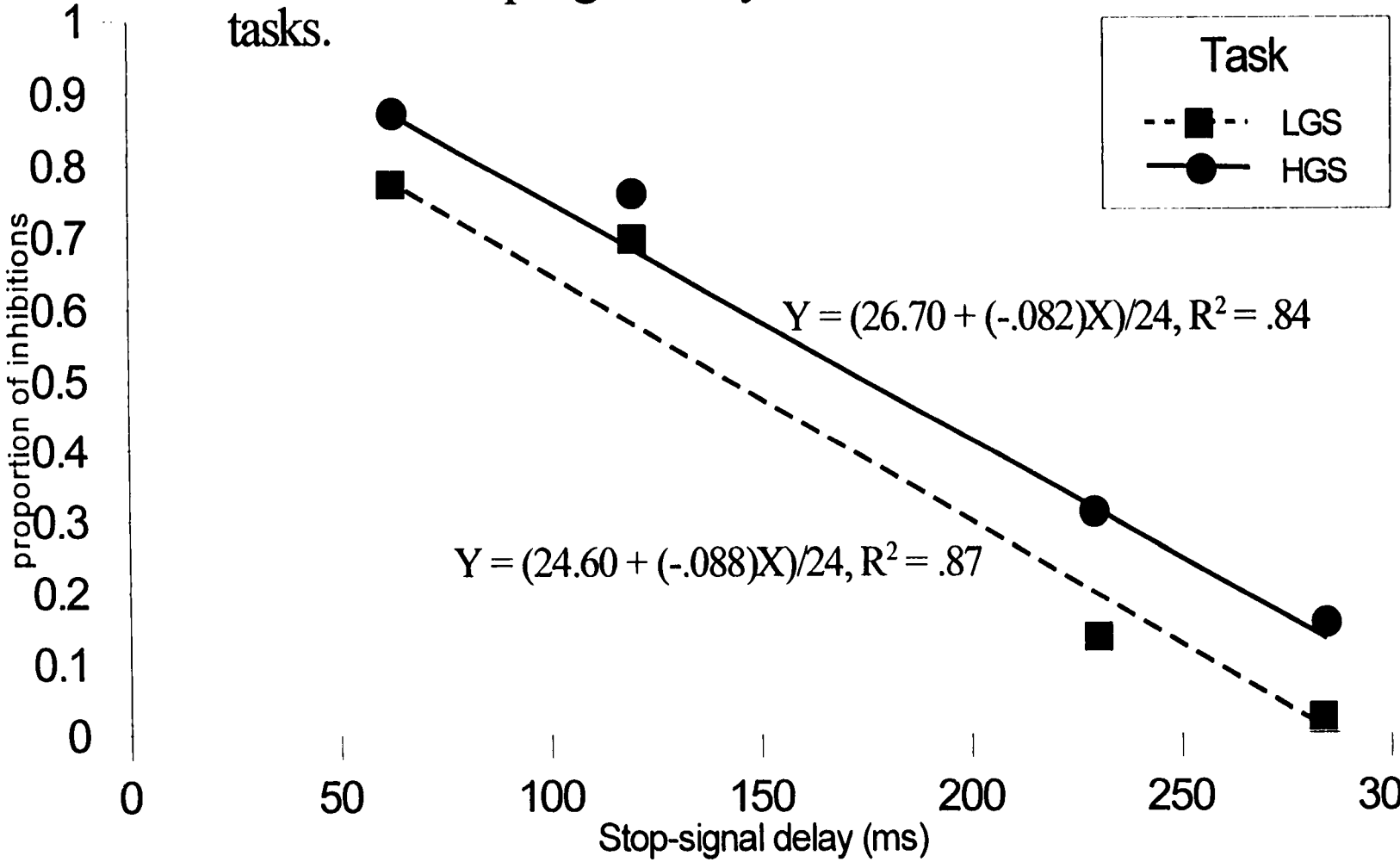
Source	SS	DF	MS	F	p
Task Load (T)	126.56	1	126.56	8.04	.025*
Error	110.19	7	15.74		
Delay (D)	3686.56	3	1228.85	290.98	.0001*
Error	88.69	21	4.22		
T X D	20.56	3	6.85	1.50	.243
Error	95.97	21	4.57		

$p<.0001$). Figure A1 plots the proportion of inhibitions observed on the 24 stop-signals at each delay on each task. Delays plotted represent the four mean stop-signal delays used on the tasks shown in Table A1a as 62, 119, 229, and 283ms . The figure indicates that more inhibitions were made on the HGS task than on the LGS task. Figure A1 also illustrates the relation between inhibitory control and stop-signal delay by showing the least-squares regression line derived from regressing the probability of inhibiting on the four mean stop-signal delays for the LGS (Table A1b) and HGS (Table A1c) tasks. Thus the evidence supports the prediction that slowing the completion of the go-signal increases inhibitory control.

Post-hoc analyses of the main effect of stop-signal delay using paired sample t-tests (with alpha correction) indicated that the number of inhibitions made at the two shortest (-1.5 and -.75 SD) stop-signal delays did not differ ($p=.14$). In contrast, there was a significant difference between the number of inhibitions made at the -.75 and +.75 SD stop-signal delays ($p<.001$) and at the +.75 and +1.5 stop-signal delays ($p<.02$). These results show that more

Figure A1

Proportion of inhibitions made at each stop-signal delay and regression lines for the proportion of inhibitions made at the stop-signal delays on the LGS and HGS tasks.

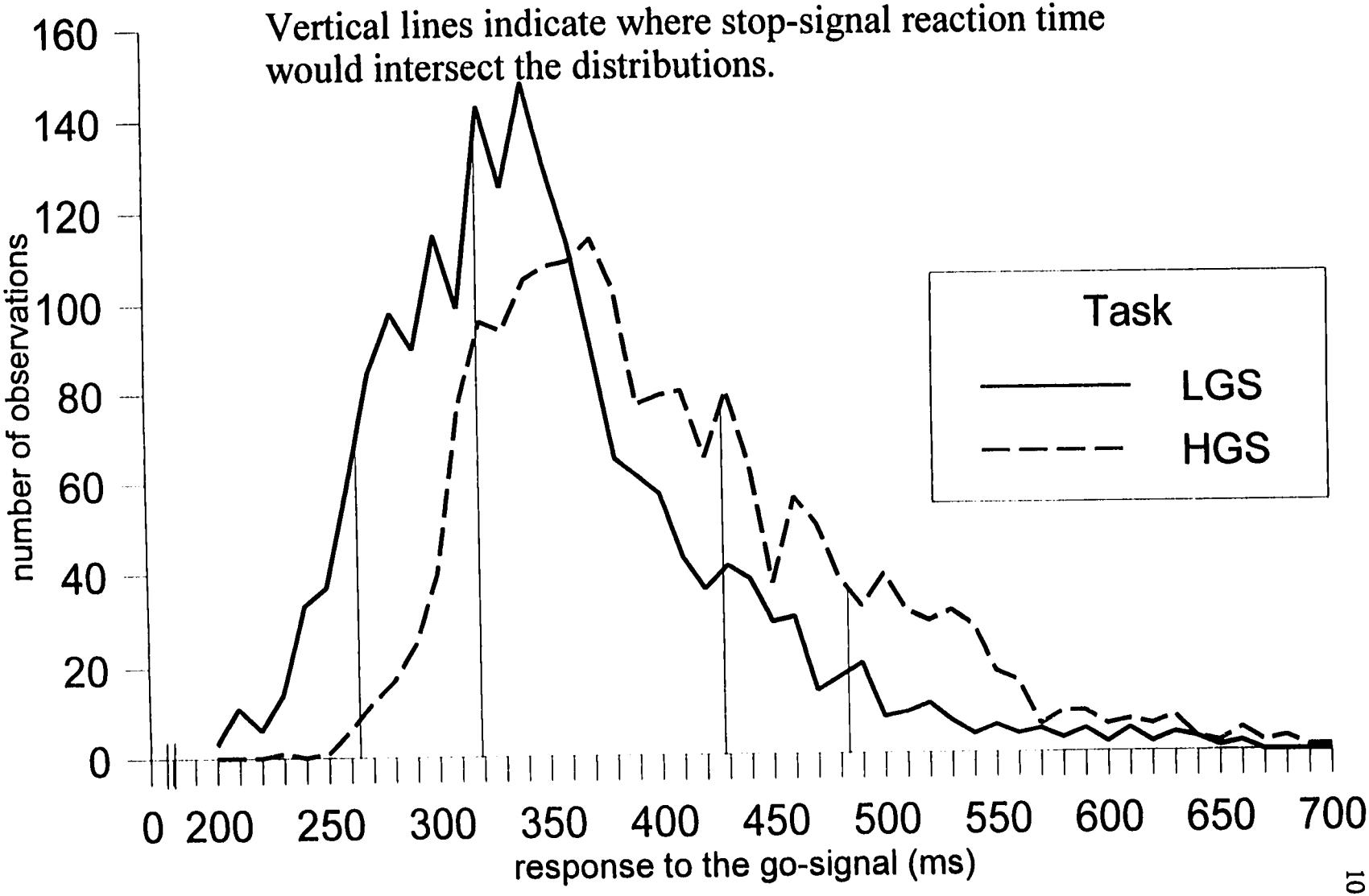


inhibitions are made when the stop-signal is placed closer in time to the go-signal on both tasks. In addition, the evidence indicates that there is little difference in the number of inhibitions made on the two shortest stop-signal delays (-1.5 and -.75). This prompted an investigation of the distribution of RTGO measures.

Each task obtained 256 RTGO measures per subject when no stop-signal was presented. Figure A2 illustrates the distribution of all RTGO measures for the LGS and HGS tasks, and reveals that the distributions of RTGO are positively skewed in both tasks. The reaction time of the stop-response must be estimated to use the information about the distribution of response times to identify appropriate stop-signal delays. Logan and Cowan (1984) developed a procedure to estimate the time of the stop-response in a number of go-stop paradigms, and reported that the average time to respond to a stop-signal is approximately 200ms (for details, see Logan & Cowan, 1984, p302). Thus, following Logan and Cowan (1984), it is possible to estimate the time required to inhibit a response to a stop-signal on the LGS and HGS. Table A1a shows that the means for the four stop-signal delay times set by the DP task were 62, 119, 229, and 283ms, respectively. By adding 200ms to the each of these mean stop-signal delays, it is possible to estimate where the completion of each stop response would intersect the RTGO distribution. For example, the first mean stop-signal delay was set at 62ms, and adding 200ms to this time would give 262ms. The number of RTGOs in the distributions of the LGS and HGS task at each estimated mean stop-signal reaction time is indicated by lines in Figure A2. These estimates and the positive skew in the RTGO measure might explain why the number of inhibitions made at the -1.5 and -.75 SD stop-signal delay intervals did not differ in either the LGS or HGS tasks. That is, the

Figure A2

Distribution of RTGO on the LGS and and HGS tasks. Vertical lines indicate where stop-signal reaction time would intersect the distributions.



positively skewed distributions of RTGO had the effect of placing the shorter stop-signal delays (-1.5, -.75 SD) closer together in the RTGO distribution than the longer stop-signal delays (+.75, +1.5 SD).

These results suggest that the method used to set the stop-signal delays in the present study did not optimize the amount of information gathered about inhibitory control. Table A5 shows the cumulative percentage of go-responses at each stop-signal delay in relation to the percentage of inhibitions at each of the stop-signal delays separately for the LGS and HGS tasks.

Table A5: The cumulative proportion of responses to the go-signal in the distributions in relation to the proportion of inhibitions made at each of the stop-signal delays on the LGS and HGS tasks:

stop-signal delay (ms)	estimated stop-signal response time (ms)	LGS		HGS	
		proportion of responses to the go-signal	proportion of inhibitions	proportion of responses to the go-signal	proportion of inhibitions
62	262	.09	.77	.01	.87
119	319	.37	.70	.15	.76
229	429	.88	.13	.70	.31
283	483	.92	.02	.85	.15

Table A5 shows that only 9% of responses to the go-signal on the LGS tasks would occur before the a mean stop-signal response time of 262ms, and that on average subjects withheld a response to the first stop-signal delay 77% of the time. As the stop-signal delay increased, the percentage of go-responses that occurred before the respond-signal reaction time also increased and the percentage of inhibitions decreased. This trend is also shown in the HGS.

From Figure A1 and Table A5, it is evident that no ceiling effect was encountered at the shortest stop-signal delay on either task. When the stop-signal was placed soon after the onset of the go-signal (mean=62ms, SD=33), subjects were able to inhibit their response a high proportion of the time on the LGS and HGS tasks (.77 and .86, respectively). In addition, there was no floor effect on inhibitions at the longest stop-signal delay (283ms) on the LGS and HGS tasks because some inhibitions were still observed. It is also evident that the two intermediate stop-signal delays were not providing maximal information about inhibitory control because inhibitions obtained from the second stop-signal delay (mean=119ms, SD=33) was similar and redundant with that of the shortest stop-signal delay. This could be corrected by placing the second stop-signal delay slightly further in time from the go-signal. The third stop-signal delay used in the pilot study (mean=229ms, SD=72) did provide useful information, but could be of greater value if it were placed sooner following the onset of the go-signal.

This experiment attempted to control individual differences among subjects by using stop-signal delay intervals standardized with respect to the mean and standard deviation of each subject's response time. However, this procedure did not optimize the information about response inhibition. In addition, such individually tailored stop-signal delays make it difficult to compare inhibitory control across subjects or between experiments (Logan, 1994). Thus, a preferable strategy is to use an appropriate range of fixed stop-signal delays for all subjects. It remains important to consider potential floor and ceiling effects when choosing these stop-signal delays. Fortunately, information on response reaction time and inhibitory control gathered in this study can guide the choice of stop-signal delay intervals. The observations

suggested that the LGS and the HGS tasks could use a short stop-signal delays of 60ms and a long stop-signal delay of 285ms, as these intervals are likely to provide useful information about inhibitory control on both tasks. To provide more information about inhibitory control at intermediate stop-signal delays, the second stop-signal delay could be placed at 135 ms and the third stop-signal delay could be placed at 210 ms following the onset of the go-signal. The relation of these four new stop-signal delays to the proportion of go-responses in the distributions from the LGS and HGS tasks in the present study can be used to estimate the number of inhibitions and go-responses that would be made at each stop-signal delay given a similar distribution of response times. These estimates are illustrated in Table A6.

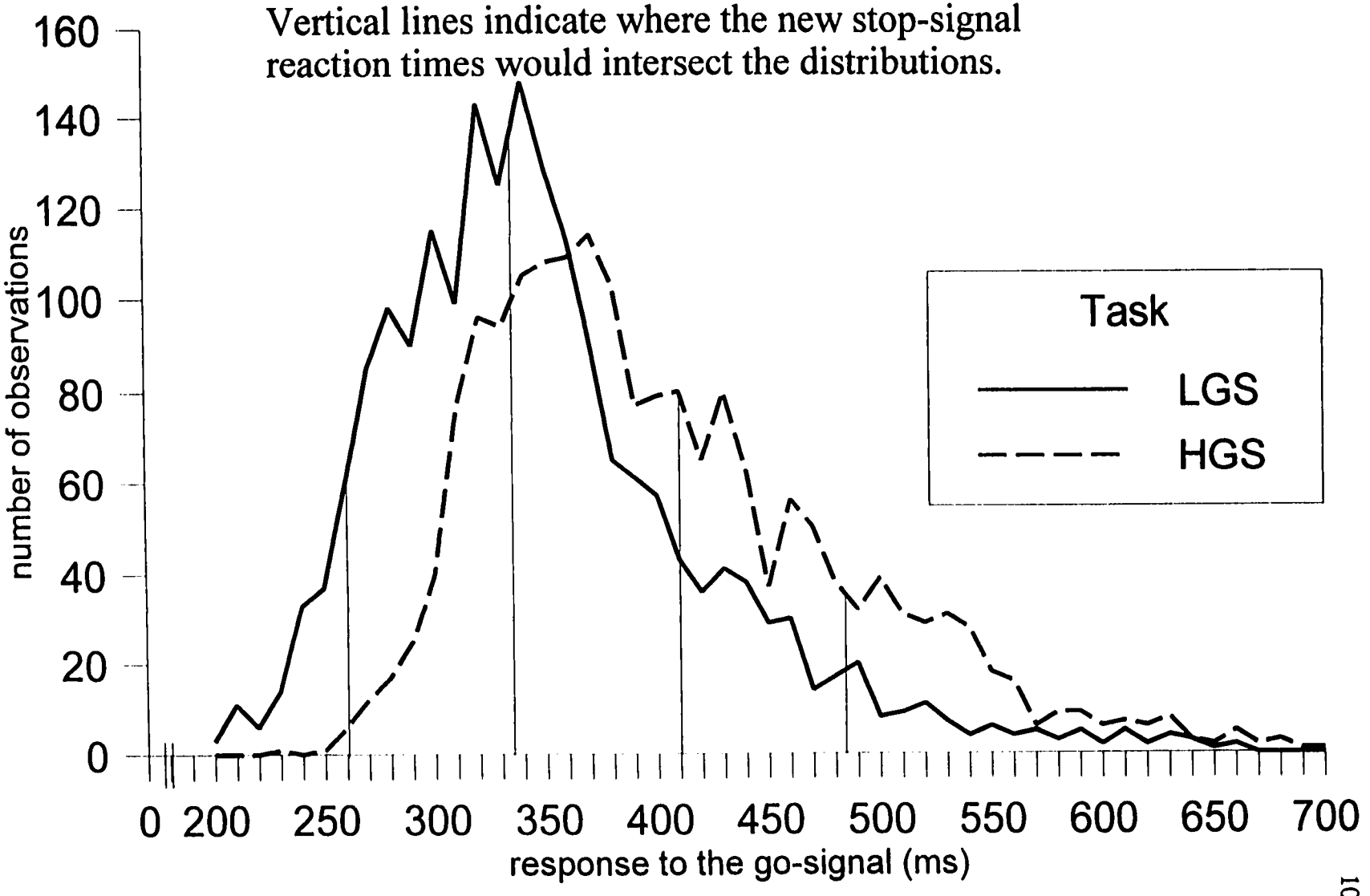
Table A6: The cumulative proportion of responses to the go-signal in the distributions in relation to the estimated proportion of inhibitions made at each of four proposed stop-signal delays on the LGS and HGS tasks:

stop-signal delay (ms)	estimated stop-signal response time (ms)	LGS		HGS	
		proportion of responses to the go-signal	estimated proportion of inhibitions	proportion of responses to the go-signal	estimated proportion of inhibitions
60	260	.09	.81	.01	.91
135	335	.51	.53	.23	.65
210	410	.84	.26	.63	.40
285	485	.95	.00	.85	.14

Figure A3 shows the distribution of RTGO on both the LGS and HGS tasks from the present study. Arrows in Figure A3 estimate where the stop-signal reaction time for each of the four new delays would intersect the RTGO distribution.

Figure A3

Distribution of RTGO on the LGS and and HGS tasks. Vertical lines indicate where the new stop-signal reaction times would intersect the distributions.



In summary, this study described the development of two parallel go-stop tasks that differed only in the time required to complete a go-response. As predicted, greater visual search to complete a response to a go-signal resulted in a slower response time and an increase in the number of inhibitions displayed to stop-signals. This study also evaluated the viability of placing stop-signal delays at intervals based on an individual's task performance. Although the results were satisfactory, it was concluded that future studies using these go-stop tasks should place stop-signals at fixed intervals for all subjects. Based on task performance in the present study, a set of stop-signal delay intervals for future studies was proposed and estimates for inhibitory control at each of these delays were given.

Appendix A1

Consent Form

I,_____, age_____ hereby state that I have volunteered to participate in a psychology study. During the session (1 hour) I will become familiar with some computer tasks measuring reaction time to a stimulus.

I understand that all records, tests and personal data are confidential, and will be used in research that does not disclose the identity of any individual.

I consent to what is proposed to be done. I agree of my own free will to participate in this experiment. The Consent is given freely and I understand that I am free to withdraw from the experiment at any time for any reason.

I understand that I shall receive a remuneration of $7 for taking part in this study.

This research is being conducted by Craig Easdon, under the supervision of the principal investigator, Dr. M. Vogel-Sprott who may be reached at the Department of Psychology, Ext. 2666.

This project has been reviewed and has received ethics clearance through the Office of Human Research of the University of Waterloo. If you have any questions or concerns about your participation, please call this Office at 885-1211, Ext. 6005.

Signed this _____ day of _____, 19____.

Participant's name_____

Participant's signature_____

Witness_____.

Appendix B

Drug-Free Study 1

Introduction

A drug-free training session served to familiarize subjects with the tasks and testing procedure to be used during the treatment session in Alcohol Study 1. This session was also designed to test the assumption of the race model of inhibitory control that go- and stop-processes are independent, and to evaluate the adequacy of the measures of inhibition obtained from the low- and high-load go-stop tasks that were developed (Appendix A).

If the go- and stop-processes are independent, then the response time to a go-signal (RTGO) should not be affected by the presence or absence of occasional stop-signals. However, if the knowledge that stop-signals will occasionally occur causes individuals to delay, or "hold back", their response to the go-signal, then RTGO should be slower under this condition compared to performance when no stop-signals are presented.

The development of a low-load go-stop task and a high-load go-stop task, described in Appendix A, led to the selection of stop-signal delays that were estimated to avoid floor and ceiling effects on measures of inhibitory control when the LGS and HGS tasks were performed. The data from this drug-free training session provided information to evaluate these estimates.

Method

Subjects

Subjects were the same sixteen right-handed males, age 19-22, who subsequently participated in Alcohol Study 1.

Apparatus

Tasks. Drug-free performance was measured on two go-stop tasks (low-load and high-load) and on two tasks that presented the low-load or high load go-signal when stop-signals were absent. All tasks were programmed using MEL, version 2.0, software (Pittsburgh, PA., 1995). All tasks were run using a 386/33 PC.

(1) Low-load go-stop task (LGS): This go-stop task was identical to the LGS described in Alcohol Study 1. A test presented 176 go-signals, 27.3% of which were followed by a stop-signal.

(2) High-load go-stop task (HGS): This task was identical to the HGS task described in Alcohol Study 1. A test presented 176 go-signals, 27.3% of which were followed by a stop-signal.

(3) Low-load go reaction time task (LRT): This task was identical to the LGS task, except that no stop-signals were presented. Instead, each test on this task simply presented 176 go-signals.

(4) High-load go reaction time task (HRT): This task was identical to the HGS task, except that no stop-signals were presented. Instead, each test on this task consisted of 176 go-signals.

The task instructions were read to the subjects and are presented in Appendix B4.

Procedure

Subjects were contacted by telephone and were informed as to the nature of the study (see Appendix B2). Subjects who expressed interest in participating in the study were scheduled for the drug-free training session. Upon arriving for the training session, subjects

were again reminded of the requirements for the study and read and signed a consent form (Appendix B3).

Subjects then performed the four tasks in one of four counterbalanced orders: (i) LRT, HRT, LGS, HGS, (ii) HRT, LRT, HGS, LGS, (iii) LGS, HGS, LRT, HRT, or (iv) HGS, LGS, HRT, LRT. Prior to performing each task, subjects were read the instructions for that task (Appendix B4). Each test was separated by a 3 minute break. Each participant performed the task alone in a room. The presentation of stimuli and recording of data were controlled by the computer. At the end of this session subjects were reminded of the requirements for the second session and were given a suggested menu to follow (Appendix B5). This session took approximately 45 minutes to complete.

Results

Independence of the go-process and the stop process.

Go-Response RT (RTGO). A 2 (task) X 2 (task load) repeated measures ANOVA of the reaction time to the go-signal (RTGO) on the four tasks revealed a main effect of task load ($F(1,15)=184.89$, $p<.0001$) (Table B1). This confirmed that, irrespective of the presence of stop-signals, the mean RTGO for the low-load tasks were faster (367.23 ms, SD=59.76) than those of the high-load tasks (435.56 ms, SD=69.42). No main effect of task or interactions were observed, thus the RTGO did not differ on go-stop and simple go reaction time tasks. As the tasks were presented in four different orders, the analysis was repeated including order as a between subjects measure. This analysis indicated no main effect of order ($F(3,12)<1$, $p=.561$) and no interactions involving order ($ps>.174$). The finding that the addition of a stopping requirement to the go reaction time tasks did not affect RTGO provides support for

the race-model's prediction that the go- and stop-process are independent.

Table B1: Repeated measures analysis of variance of drug-free response time to the go-signal on low- and high-load go-stop tasks and low- and high-load go reaction time tasks:

Source	SS	DF	MS	F	p
T	28.103	1	28.103	.021	.888
Error	20494.474	15	1366.298		
L	74571.321	1	74571.321	184.890	.0001*
Error	6049.926	15	403.328		
T X L	525.613	1	525.613	2.221	.157
Error	3549.339	15	236.623		

The accuracy of the response to the go-signal when no stop-signal was present was tested by a 2 (task) X 2 (task load) repeated measures ANOVA (Table B2). This analysis revealed main effects of task ($F(1,15)=4.33$, $p=.055$) and task load

Table B2: Repeated measures analysis of variance of drug-free response accuracy on low- and high-load go-stop tasks and low- and high-load go reaction time tasks:

Source	SS	DF	MS	F	p
Task	43.122	1	43.122	4.330	.055*
Error	149.401	15	9.960		
L	47.152	1	47.152	6.783	.020*
Error	104.274	15	6.952		
Task X L	2.151	1	2.151	.620	.443
Error	52.044	15	3.470		

($F(1,15)=6.78$, $p=.02$). The main effect of response accuracy indicated that subjects were slightly less accurate on the go-stop tasks (94.13%, SD=3.83) than on the simple go reaction time tasks (95.78%, SD=3.19). The main effect of task load indicated that subjects were

slightly less accurate on the high-load tasks (94.10%, SD=3.78) than on the low-load tasks (95.81%, SD=3.24). Although these effects were significant, the differences in accuracy are quite small (1.7%) and might simply indicate a general tendency for less accuracy on tasks that require more processing.

Inhibitions as a function of stop-signal delay in go-stop tasks.

Inhibitions. A 2 (task load) X 4 (stop-signal delay) repeated measures ANOVA of the number of inhibitions made at each of the stop-signal delays on the go-stop tasks revealed main effects of task load ($F(1,15)=14.74$, $p=.002$) and stop-signal delay ($F(3,45)=57.58$, $p<.0001$) (Table B3). The main effect of load confirmed that more inhibitions were made on

Table B3: Repeated measures analysis of variance of the number of drug-free inhibitions made at four stop-signal delays the low- and high-load go-stop tasks:

Source	SS	DF	MS	F	p
L	48.758	1	48.758	14.740	.002*
Error	49.617	15	3.308		
D	1097.852	3	365.951	57.575	.0001*
Error	286.023	45	6.356		
L X D	4.914	3	1.638	.776	.513
Error	94.961	45	2.110		

the HGS (57.8%, SD=23) than on the LGS (47.3%, SD=22). The main effect of stop-signal delay indicated that as delays were moved further from the on-set of the go-signal, less inhibitions were observed. The analysis did not reveal an interaction ($F(3,45)=.776$, $p=.513$), suggesting that the decrease in inhibitory control at the stop-signal delays did not differ as a function of the two task load conditions.

Table B4 shows the proportion of inhibitions at each stop-signal delay interval separately for the LGS and HGS tasks. The estimated proportion of inhibitions based on research in Appendix A are also shown for the purposes of comparison. Table B4 shows that the shortest stop-signal delay (60ms) on both the LGS and HGS tasks did not result in subjects withholding a response 100% of the time and the longest stop-signal delay (285ms) did not result in a complete failure to withhold a response. Thus, the stop-signal delays set for the LGS and HGS tasks successfully avoided floor and ceiling effects. The observed proportion of inhibitions shown in Table B4 illustrates the main effect of task load, and confirms that more inhibitions were displayed at each stop-signal delay on the HGS task than on the LGS task.

Table B4: The proportion of inhibitions displayed at each stop-signal delay and the estimated proportion of inhibitions at each of the stop-signal delays from Appendix A on the LGS and HGS tasks:

stop-signal delay (ms)	LGS		HGS	
	estimated proportion of inhibitions	observed proportion of. inhibitions	estimated proportion of inhibtions	observed proportion of inhibitions
60	.81	.81	.91	.89
135	.53	.60	.65	.71
210	.26	.30	.40	.46
285	.00	.18	.14	.25

Discussion

Evidence from Drug-free Study 1 supports the prediction that the go-response to low- and high-load go-signals are independent of the stop-response. The addition of stop-signals to

approximately 27% of go-trials did not significantly slow reaction time to the go-signals.

The drug-free test on the LGS and HGS tasks served to verify that more inhibitions are displayed on the high-load than on the low-load go-stop task. Moreover, this was evident at each of the four stop-signal delays that were selected on the basis of research described in Appendix A. The adequacy of the LGS task and the HGS task was indicated by the absence of floor or ceiling effects at any of the stop-signal delay intervals.

Appendix B1

Personal History Drinking Questionnaire (PDHQ)

subject #_____

Age ____ Weight _____ Height _____

Below are some questions about your personal drinking. Most ask you to answer according to what is most typical or usual for you. Please try to answer each question as honestly as possible.

1) How often, on average, do you drink alcohol? (Choose only **one**)

A) Only on special occasions, how many times per year? _____
B) Monthly, how often? _____
C) Weekly, how often? _____
D) Daily, how often? _____

2) What alcoholic beverage do you drink? _____

3) In terms of the beverage indicated in question 3, what is the **AVERAGE** quantity you drink in a single drinking occasion? (Choose only **one**)

A) WINE (estimate ounces) 1 2 3 4 5 6 7 8 9 10 or ____
B) BEER (bottles) 1 2 3 4 5 6 7 8 9 10 or ____
C) BEER (draft glasses) 1 2 3 4 5 6 7 8 9 10 or ____
D) LIQUOR (assume 1.5 ounces per drink and estimate the number of drinks) 1 2 3 4 5 6 7 8 9 10 or ____

4) How long does your typical drinking occasion last? (Choose only **one**)

A) _____ MINUTES
B) _____ HOURS
C) _____ DAYS

6) Have you ever been charged with impaired driving? YES NO

7) Have you ever experienced any problems related to your drinking? YES NO

Appendix B2

Phone Script

This is Craig Easdon calling from the University of Waterloo. Your name was among a list of students who indicated an interest in participating in payed psychology experiments. We are looking for subjects for an experiment that deals with the effect of alcohol on information processing. The experiment involves attending two sessions. The first session is drug-free and simply involves becoming familiar with some computer tasks. The second session involves performing some of the computer tasks from the first session after drinking a moderate dose of alcohol. The experiment pays $15. Are you interested in participating?

Have you ever participated in an alcohol study before?

Although the dose of alcohol used in this experiment is not harmful, it is important that you do not have any medical problems, such as diabetes. In addition, it is important that you have not had any problems related to alcohol use (e.g., prior drunk driving convictions). Similarly, it is important that you are not taking any medication: cold or allergy medications, aspirin or antihistamines, or over-the-counter drugs such as "wake-up" pills.

During the second session, when you receive alcohol, a breathalyser machine will measure your breath samples to estimate your blood alcohol concentration. During this session your blood alcohol level will not exceed 80 mg per 100 ml of blood (the legal limit).

At the end of that session your blood alcohol level may be above zero so it's important that you do not drive immediately after leaving the study.

Finally, it is important that you abstain from drinking alcohol for 24 hours prior to the session when you get alcohol. In addition, you should not eat any food during the four hours before the session and abstain from fluids, apart from sips of water, for two hours. Your stomach should be empty. Do you have any questions?

Appendix B3

Consent Form

I,_____, age_____ hereby state that I have volunteered to participate in an experiment where I might consume a moderate dose of alcohol. I understand that I will participate in two sessions. During the first session (45 min.), I will become familiar with a series of computer tasks. During the second session (2.25 hours), I will perform these same tasks under a moderate dose of alcohol. I am not currently taking any medication and will abstain from alcohol for at least 24 hours before the second session. In addition, I will fast for 3.5 hours prior to the second session to ensure that stomach contents do not affect the absorption of alcohol.

I also understand that at the conclusion of the second session my blood alcohol level might be above zero, and I must remain in the lab until it reaches a safe level.

I understand that all records, tests and personal data are confidential, and will be used in research that do not disclose the identity of any individual.

I consent to what is proposed to be done. I agree of my own free will to participate in this experiment. The Consent is given freely and I understand that I am free to withdraw from the experiment at any time for any reason.

I understand that I shall receive a remuneration of $15 for taking part in this study.

This research is being conducted by Craig Easdon under the supervision of the principal investigator, Dr. M. Vogel-Sprott who may be reached at the Department of Psychology, Ext. 2666.

This project has been reviewed and has received ethics clearance through the Office of Human Research of the University of Waterloo. If you have any questions or concerns about your participation, please call this Office at 885-1211, Ext. 6005.

Signed this _____ day of _____, 19____.

Participant's name_____

Participant's signature_____

Witness_____.

Appendix B4

Study 1: Instructions for tasks.

Low-load choice reaction time task: "In this task you will see either an "X" or an "O" appear on the computer screen before you. If you see an "X" you are to press the "?/" key as quickly as you can, and if you see an "O" you are to press the ".>" key as quickly as you can. Keep the middle finger of your right hand on the "?/" key and the index finger of your right hand on the ".>" key at all times. Try to respond as quickly and as accurately as you can."

High-load choice reaction time task: "In this task you will see a series of six letters appear on the computer screen before you. In each series of letters there will be either an "X" or an "O", if you see an "X" among the series of letters you are to press the "?/" key as quickly as you can, and if you see an "O" among the series of letters you are to press the ".>" key as quickly as you can. Keep the middle finger of your right hand on the "?/" key and the index finger of your right hand on the ".>" key at all times. Try to respond as quickly and as accurately as you can."

Low-load go-stop task: "In this task you will see either an "X" or an "O" appear on the computer screen before you. If you see an "X" you are to press the "?/" key as quickly as you can, and if you see an "O" you are to press the ".>" key as quickly as you can. Keep the middle finger of your right hand on the "?/" key and the index finger of your right hand on the ".>" key at all times. At certain times during the task you will hear a tone. When you hear the tone this means that you are not to press any key. It is still important that you respond as quickly as you can. This means that you are not to wait for the tone, but are to respond as quickly and as accurately as you can and are to withhold your response -if you can- when you do hear the tone."

High-load go-stop task: "In this task you will see a series of six letters appear on the computer screen before you. In each series of letters there will be either an "X" or an "O", if you see an "X" among the series of letters you are to press the "?/" key as quickly as you can, and if you see an "O" among the series of letters you are to press the ".>" key as quickly as you can. Keep the middle finger of your right hand on the "?/" key and the index finger of your right hand on the ".>" key at all times. At certain times during the task you will hear a tone. When you hear the tone this means that you are not to press any key. It is still important that you respond as quickly as you can. This means that you are not to wait for the tone, but are to respond as quickly and as accurately as you can and are to withhold your response -if you can- when you do hear the tone."

Appendix B5

Menu For Alcohol Sessions

Eat a light meal followed by 3.5 hours of fasting before you come in for your appointment. For example, if your appointment is at 3:30 pm, have a light snack at about 12:00 pm and then eat nothing for 3.5 hours. Below is a list of suggested foods and a list of foods to avoid. In general, avoid all dairy products and all greasy, fried foods (e.g., anything with butter). **Thank you** for your cooperation.

Suggested foods:

- breads, buns, muffins
- fruits, vegetables
- seafood (nothing packed in oil)
- meat or poultry (broiled, baked or barbecued)
- hard or soft boiled eggs
- toast with jam (no butter)
- salad (no dressing)
- sandwiches (luncheon meats, with mustard only)
- soup (not creamed)
- pickles

Foods to avoid:

- all dairy products (e.g., cheese, butter, ice-cream, margarine, yogurt or milk)
- mayonnaise
- fried eggs
- fried hamburgers
- french fries, chips
- bacon
- donuts
- peanut butter

Your next appointment is at _____. (PAS, 4th Floor)

Experimenter: Craig Easdon

Appendix C

Analyses for Alcohol Study 1

Appendix C1 Subject Characteristics

One-way analyses of variance (ANOVA) comparing age, weight, and PDHQ measures of the alcohol and placebo groups.

Age (years):

Source	SS	DF	MS	F	p
Group	2.25	1	2.25	3.316	.090
Error	9.50	14	.68		

Weight (kg):

Source	SS	DF	MS	F	p
Group	.05	1	.05	.001	.979
Error	1045.01	14	74.64		

Dose (ml alcohol/kg):

Source	SS	DF	MS	F	p
Group	.19	1	.19	.685	.422
Error	3.95	14	.28		

Frequency (weekly):

Source	SS	DF	MS	F	p
Group	.02	1	.02	.009	.927
Error	25.47	14	1.82		

Duration (hours):

Source	SS	DF	MS	F	p
Group	.190	1	.190	.080	.790
Error	35.34	14	2.52		

Appendix C1 (cont.)

Rate (dose/duration):

Source	SS	DF	MS	F	p
Group	.03	1	.034	2.208	.156
Error	.22	14	.015		

Appendix C2

Study 1: Baseline performance for number of inhibitions

Analysis of variance of the number of inhibitions made at each stop-signal delay on the LGS and HGS tasks by the alcohol and placebo groups:

Source	SS	DF	MS	F	p
Between Subjects					
Group (G)	28.125	1	28.125	.479	.500
Error	821.344	14	58.667		
Within Subjects					
Task Load (L)	84.500	1	84.500	52.651	.0001*
L X G	.031	1	.031	.019	.891
Error	22.469	14	1.605		
Delay (D)	1119.484	3	373.161	46.576	.0001*
D X G	40.266	3	13.422	1.675	.187
Error	336.500	42	8.012		
L X D	15.391	3	5.130	2.149	.108
L X D X G	11.609	3	3.870	1.621	.199
Error	100.250	42	2.387		

Table C2

Mean number of inhibitions (SD) at each stop-signal delay on the LGS and HGS tasks:

Task	Stop-signal delays			
	60ms	135ms	210ms	285ms
LGS	9.59 (3.14)	7.44 (3.65)	3.53 (3.45)	1.63 (3.18)
HGS	10.31 (2.27)	9.13 (2.55)	6.19 (4.20)	3.06 (4.02)

Appendix C3

Study 1: Baseline performance for response reaction time

Analysis of variance of response reaction time to the go-signal on the LGS and HGS tasks by the alcohol and placebo groups:

Source	SS	DF	MS	F	p
Between Subjects					
G	8294.720	1	8294.720	.908	.357
Error	127929.960	14	9137.854		
Within Subjects					
L	27881.050	1	27881.050	92.223	.0001*
L X G	217.778	1	217.778	.720	.410
Error	4232.525	14	302.323		

Study 1: Baseline performance for response accuracy

Analysis of variance of response accuracy to the go-signal on the LGS and HGS tasks by the alcohol and placebo groups:

Source	SS	DF	MS	F	p
Between Subjects					
G	67.669	1	67.669	2.314	.150
Error	409.452	14	29.247		
Within Subjects					
L	43.092	1	43.092	6.387	.024*
L X G	4.601	1	4.601	.682	.423
Error	94.448	14	6.746		

Appendix C4

Analysis of variance of the estimated drink strength by the alcohol and placebo groups:

Source	SS	DF	MS	F	p
Group	26.266	1	26.266	6.303	.025*
Error	58.344	14	4.167		

Appendix C5

Covariance analysis of the number of inhibitions made on the LGS task on three tests by the alcohol and placebo groups:

Source	SS	DF	MS	F	p
Between Subjects					
G	743.140	1	743.140	9.709	.008*
Covariate	5996.515	1	5996.515	78.341	.0001*
Error	995.068	13	76.544		
Within Subjects					
T	100.500	2	50.25	4.142	.027*
T X G	5.167	2	2.583	.213	.809
Error	339.667	28	12.131		

Adjusted mean number of inhibitions made on each of three tests on the LGS task for the alcohol and placebo groups:

Group	Test			
	30 minutes	60 minutes	90 minutes	overall test mean
Alcohol	16.19	15.47	12.21	14.62
Placebo	23.81	22.03	21.04	22.29

Appendix C5 (cont.)

Covariance analysis of the number of inhibitions made on the HGS task on three tests by the alcohol and placebo groups:

Source	SS	DF	MS	F	p
Between Subjects					
G	404.190	1	404.190	15.340	.002*
Covariate	4670.754	1	4670.754	177.265	.0001*
Error	342.538	13	26.349		
Within Subjects					
T	199.500	2	99.750	7.267	.003*
T X G	45.500	2	22.750	1.657	.209
Error	384.333	28	13.726		

Adjusted mean number of inhibitions made on each of three tests on the HGS task for the alcohol and placebo groups:

Group	Test			
	30 minutes	60 minutes	90 minutes	overall test mean
Alcohol	25.96	23.25	19.01	22.74
Placebo	29.67	29.37	26.87	28.64

Appendix C6

Covariance analysis for response reaction time to the go-signal on three tests of the LGS task by the alcohol and placebo groups:

Source	SS	DF	MS	F	p
Between Subjects					
G	2898.067	1	2898.067	1.612	.226
Covariate	249412.554	1	249412.554	138.752	.0001*
Error	23368.023	13	1797.54		
Within Subjects					
T	278.013	2	139.006	.703	.503
T X G	893.152	2	446.576	2.260	.123
Error	5534.003	28	197.643		

Adjusted means of reaction time to the go-signal (ms) on three tests of the LGS task by the alcohol and placebo groups:

Group	Test			
	30 minutes	60 minutes	90 minutes	overall test mean
Alcohol	375.22	383.35	376.20	378.26
Placebo	370.14	358.98	357.77	362.30

Appendix C6 (cont.)

Covariance analysis for response reaction time to the go-signal on three tests of the HGS by the alcohol and placebo groups:

Source	SS	DF	MS	F	p
Between Subjects					
G	2835.043	1	2835.043	1.180	.297
Covariate	291152.362	1	291152.362	121.183	.0001*
Error	31233.538	13	2402.580		
Within Subjects					
T	902.366	2	451.183	.838	.443
T X G	492.195	2	246.097	.457	.638
Error	15080.305	28	538.582		

Adjusted means of reaction time to the go-signal (ms) on three tests of the HGS task by the alcohol and placebo groups:

Group	Test			
	30 minutes	60 minutes	90 minutes	overall test mean
Alcohol	438.98	452.45	436.02	442.48
Placebo	428.82	427.79	423.10	426.57

Appendix C7

Analysis of variance of response accuracy to the go-signal on three tests on the LGS and HGS tasks by the alcohol and placebo groups:

Source	SS	DF	MS	F	p
Between Subjects					
G	25.950	1	25.950	1.328	.268
Error	273.469	14	19.533		
Within Subjects					
L	93.008	1	93.008	4.685	.048*
L X G	1.518	1	1.518	.076	.786
Error	277.920	14	19.851		
T	29.067	2	14.534	1.613	.217
T X G	39.702	2	19.851	2.203	.129
Error	252.331	28	9.012		
L X T	21.852	2	10.926	1.525	.235
L X T X G	32.094	2	16.047	2.239	.125
Error	200.638	28	7.166		

Appendix C8

Covariance analysis of response accuracy to the go-signal on three tests of the LGS task by the alcohol and placebo groups:

Source	SS	DF	MS	F	p
Between Subjects					
G	15.306	1	15.306	.597	.454
Covariate	764.363	1	764.363	29.811	.0001*
Error	333.325	13	25.640		
Within Subjects					
T	43.934	2	21.967	2.643	.089
T X G	65.452	2	32.726	3.938	.031*
Error	232.691	28	9.310		

Adjusted means for response accuracy (% correct) on three tests on the LGS task by the alcohol and placebo groups:

Group	Test			
	30 minutes	60 minutes	90 minutes	overall test mean
Alcohol	91.71	94.15	91.78	92.55
Placebo	96.04	93.37	91.80	93.74

Appendix C8 (cont.)

Covariance analysis of response accuracy to the go-signal on three tests of the HGS task by the alcohol and placebo groups:

Source	SS	DF	MS	F	p
Between Subjects					
G	2.397	1	2.397	.204	.659
Covariate	587.623	1	587.623	50.107	.0001*
Error	152.454	13	11.727		
Within Subjects					
T	6.986	2	3.493	.444	.646
T X G	6.344	2	3.172	.403	.672
Error	220.279	28	7.867		

Adjusted means for response accuracy (% correct) to the go-signal on the HGS by the alcohol and placebo groups:

Group	Test			
	30 minutes	60 minutes	90 minutes	overall test mean
Alcohol	91.94	92.52	93.19	92.55
Placebo	92.88	94.10	92.11	93.03

Appendix C9

Mean change in inhibitions as a function of stop-signal delay on the LGS and HGS task by the alcohol and placebo groups:

Group	Task	stop-signal delay (ms)			
		60	135	210	285
Alcohol	LGS	-3.31	-2.92	-.40	-.38
	HGS	-1.54	-1.67	-1.46	-1.33
Placebo	LGS	1.08	-.08	-1.00	.29
	HGS	-.17	.00	-.13	.29

Adjusted mean number of inhibitions as a function of stop-signal delay on the LGS and HGS task by the alcohol and placebo groups:

Group	Task	stop-signal delay (ms)			
		60	135	210	285
Alcohol	LGS	6.12	4.22	2.55	1.21
	HGS	8.66	7.35	4.78	1.75
Placebo	LGS	10.85	7.24	3.11	1.96
	HGS	10.25	9.23	6.01	3.33

Appendix C10

Analysis of variance of the change in number of inhibitions made at each stop-signal delay on the LGS by the alcohol and placebo groups:

Source	SS	DF	MS	F	p
Between Subjects					
G	59.418	1	59.418	9.734	.008*
Error	85.455	14	6.104		
Within Subjects					
D	23.627	3	7.876	3.038	.039*
D X G	63.363	3	21.121	8.148	.001*
Error	108.872	42	2.592		

Analysis of variance of the change in number of inhibitions made at each stop-signal delay on the HGS by the alcohol and placebo groups:

Source	SS	DF	MS	F	p
Between Subjects					
G	36.000	1	36.000	17.446	.001*
Error	28.889	14	2.063		
Within Subjects					
D	1.153	3	.384	.158	.924
D X G	.347	3	.116	.048	.986
Error	102.056	42	2.430		

Appendix C11

Analysis of variance of the change in number of inhibitions made at the three earliest stop-signal delays on three tests on both the LGS and HGS by the alcohol and placebo groups:

Source	SS	DF	MS	F	p
Between Subjects					
Group	242.000	1	242.000	14.753	.002*
Error	229.653	14	16.404		
Within Subjects					
L	5.556	1	5.556	1.079	.317
L X G	10.125	1	10.125	1.966	.183
Error	72.097	14	5.150		
T	80.840	2	40.420	18.020	.0001*
T X G	17.021	2	8.510	3.794	.035*
Error	62.806	28	2.243		
D	8.595	2	4.298	.429	.655
D X G	82.505	2	41.253	4.118	.027*
Error	280.483	28	10.017		
L X T	2.965	2	1.483	.362	.699
L X T X G	4.464	2	2.323	.567	.573
Error	114.611	28	4.093		
L X D	6.950	2	3.475	.649	.530
L X D X G	75.318	2	37.659	7.036	.003*
Error	149.872	28	5.353		
T X D	5.139	4	1.285	.604	.661
T X D X G	5.708	4	1.427	.671	.615
Error	119.153	56	2.128		
L X T X D	13.139	4	3.285	1.994	.108
L X T X D X G	5.708	4	1.427	.866	.490
Error	92.264	56	1.648		

Appendix D

Drug-Free Study 2

Introduction

A drug-free training session familiarized subjects with the tasks and testing procedure to be used during in Alcohol Study 2. The performance data obtained during this drug-free session was used to test predictions about the reaction time to go-signals and the number of inhibitions on low- and high-load go-stop tasks and low- and high-load change tasks. Logan (1994) has reported that drug-free response time to a go-signal is slightly slower on change paradigms than on go-stop paradigms, and likely results from the additional processing requirements of the change paradigm. Furthermore, Logan and Burkell (1986) observed that response time to reengage a second response was slower after a failure to inhibit than after an inhibition. This makes sense because when there is a failure to inhibit, the first response to the go-signal continues and might compete with the reengagement of a second response. Conversely, when the first response is halted, there should be less competition for the reengagement of the second response.

This drug-free session tested the following predictions:

(1) if the change paradigm tasks require greater processing than the go-stop paradigm tasks, then response time to the go-signal should be slower on the change tasks than on the go-stop tasks.

(2) if response time to the go-signal is slower on the change tasks, then the assumption of independence between the go- and stop-process predicts that more inhibitions should be observed on the change tasks than on the go-stop tasks.

(3) if a failure to inhibit a response interferes with switching and completing a second response, then response reaction time to reengage a response should be slower on trials where there is a failure to inhibit than on trials where inhibition is successful.

Method

Subjects

Subjects in this study were the same sixteen right-handed males who participated in Alcohol Study 2.

Apparatus

Tasks. The drug-free performance of each subject was measured on two go-stop tasks (low-load and high-load) and on two change tasks (low-load and high load). The change tasks were identical to those described in Alcohol Study 2. A test consisted of 176 trials, 50 of which were followed by a stop-signal at one of five delays (0, 60, 135, 210, 285ms). The only difference between the go-stop and change tasks was that the change tasks required subjects to make a different button press response to the stop-signal. The go-stop and change tasks provided measures of the number of inhibitions made at each stop-signal delay, and response time to the go-signal (RTGO). The change tasks also measured response flexibility by recording the reaction time to the second response after inhibitions (RT2 inhibit) and failures to inhibit (RT2 fail). Thus, all subjects performed the four tasks on this drug-free session: low-load change task (LC), high-load change task (HC), low-load go-stop task (LGS), and high-load go-stop task (HGS).

Procedure

Subjects were contacted by telephone and were informed as to the nature of the study.

If subjects agreed to participate in the study, then the drug-free training session was scheduled. Upon arriving for this session, subjects were again reminded of the requirements for the study and read and signed a consent form.

An equal number of subjects then performed the four tasks in one of four counterbalanced orders: (i) LGS, HGS, LC, HC, (ii) HGS, LGS, HC, LC, (iii) LC, HC, LGS, HGS, or (iv) HC, LC, HGS, LGS. Prior to performing each task, subjects were read the instructions for that task (Appendix D1). Each test was separated by a 3 minute break. Each participant performed the task alone in a room. The presentation of stimuli and recording of data were controlled by the computer. This session took approximately 45 minutes to complete.

Results

Go-Response RT (RTGO). A 2 (task) X 2 (task load) repeated measures ANOVA of RTGO indicated main effects of task ($F(1,15)=6.84$, $p=.02$) and task load ($F(1,15)=110.59$, $p=.0001$) (Table D1). The main effect of task confirmed the prediction that response time on

Table D1: Repeated measures analysis of variance of drug-free response reaction time to the go-signal on low- and high-load go-stop tasks and low- and high-load change tasks:

Source	SS	DF	MS	F	p
Task	4691.051	1	4691.051	6.839	.020*
Error	10289.600	15	685.973		
L	157820.473	1	157820.473	110.586	.0001*
Error	21406.993	15	1427.133		
Task X L	21.448	1	21.448	.053	.821
Error	6093.442	15	406.229		

the change tasks would be slower (447.30ms; SD=61.08) than response time on the go-stop tasks (430.18ms; SD=59.83). The main effect of load replicated previous findings showing that response time is slower on the high-load tasks (488.40ms; SD=72.35) than on the low-load tasks (389.08ms; 49.45).

Response accuracy on the four tasks was checked by a 2 (task) X 2 (task load) repeated measures ANOVA (Table D2). This analysis contained a main effect of task load ($F(1,15)=6.92$, $p=.019$), and supported previous findings that response accuracy was slightly better on the low-load task (95.29%; SD=4.47) than on the high-load task (93.67%; SD=4.73). The lack of a significant main effect of task suggested that response accuracy did not depend on whether or not subjects were required to make a second response.

Table D2: Repeated measures analysis of variance of drug-free response accuracy on low- and high-load go-stop tasks and low- and high change tasks:

Source	SS	DF	MS	F	p
Task	34.369	1	34.369	1.187	.293
Error	434.249	15	28.950		
L	42.413	1	42.413	6.923	.019*
Error	91.895	15	6.126		
Task X L	10.160	1	10.160	1.576	.229
Error	96.727	15	6.448		

Inhibitions. A 2 (task) X 2 (task load) X 5 (stop-signal delay) repeated measures ANOVA of the number of inhibitions made at each stop-signal delay on the tasks revealed main effects of task load ($F(1,15)=8.91$, $p=.009$) and stop-signal delay ($F(4,60)=59.48$, $p=.0001$) (Table D3). The main effect of load replicated findings that more inhibitions are

made on high-load (mean=30.78; SD=11.07) tasks than on low-load tasks (mean=24.94; 10.36). The main effect of stop-signal delay indicated that fewer inhibitions were made as the delays were placed further in time from the go-signal.

Table D3: Repeated measures analysis of variance of the number of drug-free inhibitions made at each stop-signal delay on low-load and high-load change tasks:

Source	SS	DF	MS	F	p
Task (T)	37.128	1	37.128	2.164	.162
Error	257.322	15	17.155		
L	109.278	1	109.278	8.910	.009*
Error	183.972	15	12.265		
D	1139.863	4	284.966	59.484	.0001*
Error	287.432	60	4.791		
T X L	.153	1	.153	.029	.868
Error	80.097	15	5.340		
T X D	10.700	4	2.675	1.320	.273
Error	121.600	60	2.027		
L X D	17.050	4	4.263	.1.723	.157
Error	148.450	60	2.474		
T X L X D	8.238	4	2.059	1.502	.213
Error	82.263	60	1.371		

The absence of a task effect ($F(1,15)=2.16$, $p=.16$) in Table D3 does not support the prediction that more inhibitions would be made on the change tasks than on the go-stop tasks.

Response Flexibility (RT2). The response time of a second response on the change tasks following either a successful or unsuccessful inhibition was tested by a 2 (task load) X 2 (flexibility) repeated measures ANOVA (Table D4).

Table D4: Repeated measures analysis of variance of drug-free response flexibility (RT2) after inhibitions and failure to inhibit on the low- and high-load change tasks:

Source	SS	DF	MS	F	p
L	43590.654	1	43590.654	7.852	.013*
Error	83276.976	15	5551.798		
Flexibility (F)	93158.485	1	93158.485	6.959	.019*
Error	200800.213	15	13386.681		
L X F	165.347	1	165.347	.041	.842
Error	60326.931	15	4021.795		

This analysis indicated main effects of task load ($F(1,15)=7.85$, $p=.013$) and flexibility ($F(1,15)=6.96$, $p=.019$). The main effect of load indicated that time to reengage the second response was slower on the high-load task (502.83ms; SD=79.53) than on the low-load task (450.63ms; SD=79.15)). This finding is consistent with the notion that the degree of processing required to complete a first response can influence the performance of a second response. The main effect of flexibility confirmed the prediction that the reaction time of the second response would be slower following a failure to inhibit (514.88ms, SD=98.70) than following an inhibition (438.58; SD=100.02). This finding supports the hypothesis that making a first response interferes with making a second response.

Discussion

This study compared performance on two change tasks and two go-stop tasks. Results indicated that response reaction time to the go-signal was slower on the change tasks than on the go-stop tasks, thus confirming the prediction that having to make an additional response to a stop-signal slows the completion of the go-response. The prediction that slowing the

completion of the go-response would result in more inhibitory control on the change tasks was not supported. This might have resulted because the response time to the go-signal on the change tasks was only slightly slower than that on the go-stop tasks (approximately 18 ms), which resulted in only a slight shift in the response time distribution that might have been too small to influence the number of inhibitions made.

This study also confirmed that the reaction time of a second response is longer following a failure to withhold the first response than when the first response is inhibited. This result supports the notion that making a first response interferes with the time to complete a second response. There was also evidence that the processing load demands of a first response can interfere with the completion of a second response, as reaction time to make a second response was slower in the high-load condition than in the low-load condition.

Appendix D1

Study 2: Instructions for tasks.

Low-load go-stop task: "In this task you will see either an "X" or an "O" appear on the computer screen before you. If you see an "X" you are to press the "?/" key as quickly as you can, and if you see an "O" you are to press the ".>" key as quickly as you can. Keep the middle finger of your right hand on the "?/" key and the index finger of your right hand on the ".>" key at all times. At certain times during the task you will hear a tone. When you hear the tone this means that you are not to press any key. It is still important that you respond as quickly as you can. This means that you are not to wait for the tone, but are to respond as quickly and as accurately as you can and are to withhold your response -if you can- when you do hear the tone."

High-load go-stop task: "In this task you will see a series of six letters appear on the computer screen before you. In each series of letters there will be either an "X" or an "O", if you see an "X" among the series of letters you are to press the "?/" key as quickly as you can, and if you see an "O" among the series of letters you are to press the ".>" key as quickly as you can. Keep the middle finger of your right hand on the "?/" key and the index finger of your right hand on the ".>" key at all times. At certain times during the task you will hear a tone. When you hear the tone this means that you are not to press any key. It is still important that you respond as quickly as you can. This means that you are not to wait for the tone, but are to respond as quickly and as accurately as you can and are to withhold your response -if you can- when you do hear the tone."

Low-load change task: "In this task you will see either an "X" or an "O" appear on the computer screen before you. If you see an "X" you are to press the "?/" key as quickly as you can, and if you see an "O" you are to press the ".>" key as quickly as you can. Keep the middle finger of your right hand on the "?/" key and the index finger of your right hand on the ".>" key at all times. At certain times during the task you will hear a tone. When you hear the tone this means that you are not to press any key with your right hand. It is still important that you respond as quickly as you can. This means that you are not to wait for the tone, but are to respond as quickly and as accurately as you can and are to withhold your response -if you can- when you do hear the tone. In this task whenever you hear a tone, you should also try to press the "Z" key as quickly as you can with the index finger of your left hand."

High-load change task: "In this task you will see a series of six letters appear on the computer screen before you. In each series of letters there will be either an "X" or an "O", if you see an "X" among the series of letters you are to press the "?/" key as quickly as you can, and if you see an "O" among the series of letters you are to press the ".>" key as quickly as you can. Keep the middle finger of your right hand on the "?/" key and the index finger of your right hand on the ".>" key at all times. At certain times during the task you will hear a tone. When you hear the tone this means that you are not to press any key. It is still important that you

respond as quickly as you can. This means that you are not to wait for the tone, but are to respond as quickly and as accurately as you can and are to withhold your response -if you can- when you do hear the tone. In this task whenever you hear a tone, you should also try to press the "Z" key as quickly as you can with the index finger of your left hand."

Appendix E

Analyses for Alcohol Study 2

Appendix E1

Subject Characteristics

One-way analyses of variance (ANOVAs) comparing age, weight, and PDHQ measures of the alcohol and placebo groups.

Age (years):

Source	SS	DF	MS	F	p
Group	3.062	1	3.062	1.460	.247
Error	29.375	14	2.098		

Weight (kg):

Source	SS	DF	MS	F	p
Group	37.669	1	37.669	.214	.651
Error	2460.682	14	175.763		

Dose (ml alcohol/kg):

Source	SS	DF	MS	F	p
Group	.004	1	.004	.012	.914
Error	4.070	14	.291		

Duration (hours):

Source	SS	DF	MS	F	p
Group	.766	1	.766	.245	.628
Error	43.719	14	3.123		

Appendix E1 (cont.)

Frequency (weekly):

Source	SS	DF	MS	F	p
Group	1.891	1	1.891	.640	.437
Error	41.344	14	2.953		

Rate (dose/duration):

Source	SS	DF	MS	F	p
Group	.163	1	.163	1.034	.326
Error	2.199	14	.157		

Appendix E2

Study 2: Baseline response flexibility (RT2)

Analysis of variance of the drug-free RT2 following inhibitions or failures to inhibit on the low-load and high-load change tasks by the alcohol and placebo groups:

Source	SS	DF	MS	F	p
Between Subjects					
G	1563.708	1	1563.708	.107	.749
Error	204964.307	14	14640.308		
Within Subjects					
L	9757.241	1	9757.241	5.778	.031*
L X G	4060.079	1	4060.079	2.404	.143
Error	23641.717	14	1688.694		
Flexibiltity (F)	40771.182	1	40771.182	10.245	.006*
F X G	6717.237	1	6717.237	1.688	.215
Error	55715.904	14	55715.904		
L X F	7852.397	1	7852.397	10.466	.006*
L X F X G	9.023	1	9.023	.012	.914
Error	10524.254	14	751.732		

Appendix E3

Study 2: Baseline performance for number of inhibitions

Analysis of variance of the number of inhibitions made at each stop-signal delay on the LC and HC tasks by the alcohol and placebo groups:

Source	SS	DF	MS	F	p
Between Subjects					
Group (G)	.025	1	.025	.001	.978
Error	464.95	14	33.211		
Within Subjects					
Task Load (L)	57.600	1	57.600	18.581	.001*
L X G	.400	1	.400	.129	.725
Error	43.400	14	3.100		
Delay (D)	797.413	4	199.353	58.319	.0001*
D X G	11.163	4	2.791	.816	.520
Error	191.425	56	3.418		
L X D	14.838	4	3.709	2.003	.107
L X D X G	3.038	4	.759	.410	.801
Error	103.725	56	1.852		

Table E3

Mean number of inhibitions (SD) at each stop-signal delay on the LC and HC tasks:

Task	Stop-signal delays				
	0ms	60ms	135ms	210ms	285ms
LC	8.06 (1.81)	6.94 (1.69)	5.38 (2.60)	2.75 (2.70)	1.44 (2.03)
HC	8.38 (1.15)	7.69 (2.33)	6.75 (2.38)	4.81 (2.74)	2.94 (3.21)

Appendix E4

Study 2: Baseline performance of response reaction time

Analysis of variance of response reaction time to the go-signal on the LC and HC tasks prior to drinking by the alcohol and placebo groups:

Source	SS	DF	MS	F	p
Between Subjects					
G	1192.917	1	1192.917	.202	.660
Error	82681.040	14	5905.789		
Within Subjects					
L	57777.902	1	57777.902	120.489	.0001*
L X G	29.147	1	29.147	.061	.809
Error	6713.380	14	479.527		

Study 2: Baseline performance of response accuracy

Analysis of variance of response accuracy to the go-signal on the LC and HC tasks prior to drinking by the alcohol and placebo groups:

Source	SS	DF	MS	F	p
Between Subjects					
G	7.125	1	7.125	.441	.518
Error	226.324	14	16.166		
Within Subjects					
L	27.938	1	27.938	13.731	.002*
L X G	4.133	1	4.133	2.031	.176
Error	28.484	14	2.035		

Appendix E5

Beverage strength rating

Analysis of variance of the estimated drink strength by the alcohol and placebo groups:

Source	SS	DF	MS	F	p
Group	22.563	1	22.563	10.939	.005*
Error	28.875	14	2.063		

Appendix E6

Covariance analysis of flexibility (RT2) following successful inhibitions on three tests of the LC task by the alcohol and placebo groups:

Source	SS	DF	MS	F	p
Between Subjects					
G	15.31	1	15.31	.003	.957
Covariate	42730.506	1	42730.506	8.339	.013*
Error	66616.233	13	5124.326		
Within Subjects					
T	759.382	2	379.691	.540	.589
T X G	522.536	2	261.268	.372	.693
Error	19681.992	28	702.928		

Adjusted means of RT2 (ms) following successful inhibitions on three tests of the LC task by the alcohol and placebo groups:

Group	Test			
	30 minutes	60 minutes	90 minutes	overall test mean
Alcohol	385.57	383.52	385.15	384.75
Placebo	388.05	390.66	371.74	383.48

Appendix E6 (cont.)

Covariance analysis of flexibility (RT2) following failures to inhibit on three tests of the LC task by the alcohol and placebo groups:

Source	SS	DF	MS	F	p
Between Subjects					
G	24509.465	1	24509.465	2.309	.153
Covariate	92828.790	1	92828.790	8.745	.011*
Error	137999.787	13	10615.368		
Within Subjects					
T	28.288	2	14.144	.021	.979
T X G	185.123	2	92.561	.139	.871
Error	18634.787	28	665.528		

Adjusted means of RT2 following failures to inhibit on three tests of the LC task by the alcohol and placebo groups:

Group	Test			
	30 minutes	60 minutes	90 minutes	overall test mean
Alcohol	471.01	469.72	463.80	468.18
Placebo	421.77	421.43	425.23	422.81

Appendix E6 (cont.)

Covariance analysis of flexibility (RT2) following successful inhibitions on three tests of the HC task by the alcohol and placebo groups:

Source	SS	DF	MS	F	p
Between Subjects					
G	328.336	1	328.336	.068	.799
Covariate	56720.769	1	56720.769	11.715	.005*
Error	62942.003	13	4841.693		
Within Subjects					
T	6999.706	2	3499.853	3.581	.041*
T X G	2692.122	2	1346.061	1.377	.269
Error	27364.997	28	977.321		

Adjusted means of RT2 following successful inhibitions on three tests of the HC task by the alcohol and placebo groups:

Group	Test			
	30 minutes	60 minutes	90 minutes	overall test mean
Alcohol	421.52	395.81	373.60	396.98
Placebo	406.31	405.17	395.15	402.21

Appendix E6 (cont.)

Covariance analysis of flexibility (RT2) following failures to inhibit on three tests of the HC task by the alcohol and placebo groups:

Source	SS	DF	MS	F	p
Between Subjects					
G	35323.347	1	35323.347	4.614	.051*
Covariate	122735.708	1	122735.708	16.032	.002*
Error	99526.228	13	7655.864		
Within Subjects					
T	1697.960	2	848.980	.604	.553
T X G	3143.489	2	1571.744	1.119	.341
Error	39326.138	28	1404.505		

Adjusted means of RT2 following failures to inhibit on three tests of the HC task by the alcohol and placebo groups:

Group	Test			
	30 minutes	60 minutes	90 minutes	overall test mean
Alcohol	494.31	518.88	488.67	500.62
Placebo	436.75	441.14	454.01	443.97

Appendix E7

Covariance analysis of the number of inhibitions on three tests on the LC task by the alcohol and placebo groups:

Source	SS	DF	MS	F	p
Between Subjects					
G	827.921	1	827.921	14.224	.002*
Covariate	3658.972	1	3658.972	62.861	.0001*
Error	756.695	13	58.207		
Within Subjects					
T	30.875	2	15.438	1.395	.265
T X G	5.292	2	2.646	.239	.789
Error	309.833	28	11.065		

Adjusted mean number of inhibitions on each of three tests on the LC task by the alcohol and placebo groups:

Group	Test			
	30 minutes	60 minutes	90 minutes	overall test mean
Alcohol	14.31	15.41	17.06	15.59
Placebo	23.44	23.72	24.57	23.91

Appendix E7 (cont.)

Covariance analysis of the number of inhibitions on three tests of the HC task by the alcohol and placebo groups:

Source	SS	DF	MS	F	p
Between Subjects					
G	381.128	1	381.128	3.653	.078
Covariate	3932.523	1	3932.523	37.688	.0001*
Error	1356.477	13	104.344		
Within Subjects					
T	6.000	2	3.000	.211	.811
T X G	8.000	2	4.000	.281	.757
Error	398.000	28	14.214		

Adjusted mean number of inhibitions on each of three tests on the HC task by the alcohol and placebo groups:

Group	Test			
	30 minutes	60 minutes	90 minutes	overall test mean
Alcohol	26.44	25.17	24.68	24.43
Placebo	31.06	30.83	31.32	31.07

Appendix E8

Covariance analysis for response reaction time to the go-signal on three tests of the LC task by the alcohol and placebo groups:

Source	SS	DF	MS	F	p
Between Subjects					
G	592.632	1	592.632	.484	.499
Covariate	65221.555	1	65221.555	53.223	.0001*
Error	15930.774	13	1225.444		
Within Subjects					
T	1657.036	2	828.518	3.013	.065
T X G	1050.631	2	525.315	1.910	.167
Error	7700.503	28	275.018		

Adjusted means of reaction time to the go-signal (ms) on three tests of the LC task by the alcohol and placebo groups:

Group	Test			
	30 minutes	60 minutes	90 minutes	overall test mean
Alcohol	388.25	399.80	410.69	399.58
Placebo	387.37	398.57	391.58	392.51

Appendix E8 (cont.)

Covariance analysis for response reaction time to the go-signal on three tests of the HC task by the alcohol and placebo groups:

Source	SS	DF	MS	F	p
Between Subjects					
G	4773.144	1	4773.144	2.033	.177
Covariate	165387.327	1	165387.327	70.443	.0001*
Error	30521.464	13	2347.805		
Within Subjects					
T	645.285	2	322.642	.891	.422
T X G	1198.183	2	599.091	1.654	.211
Error	10141.811	28	362.208		

Adjusted means of reaction time to the go-signal (ms) on three tests of the HC task by the alcohol and placebo groups:

Group	Test			
	30 minutes	60 minutes	90 minutes	overall test mean
Alcohol	480.27	486.87	500.06	489.07
Placebo	468.49	471.84	466.62	468.98

Appendix E9

Analysis of variance of the change in response accuracy to the go-signal on three tests of the LC and HC tasks by the alcohol and placebo groups:

Source	SS	DF	MS	F	p
Between Subjects					
G	82.325	1	82.325	3.729	.074
Error	309.063	14	22.076		
Within Subjects					
L	.193	1	.193	.023	.883
L X G	6.668	1	6.668	.783	.391
Error	119.245	14	8.517		
T	15.411	2	7.705	1.156	.329
T X G	39.731	2	19.865	2.981	.067
Error	186.605	28	6.664		
L X T	15.261	2	7.630	1.115	.342
L X T X G	61.131	2	30.565	4.465	.021*
Error	191.688	28	6.846		

Appendix E10

Analysis of the change in response accuracy to the go-signal on three tests of the LC task by the alcohol and placebo groups:

Source	SS	DF	MS	F	p
Between Subjects					
G	67.925	1	67.925	10.299	.006*
Error	92.336	14	6.595		
Within Subjects					
T	20.412	2	10.206	3.300	.052*
T X G	10.347	2	5.173	1.673	.206
Error	86.595	28	3.093		

Mean change in response accuracy (%) on three tests of the LC task by the alcohol and placebo groups:

Group	Test			
	30 minutes	60 minutes	90 minutes	overall test mean
Alcohol	-3.38	-2.90	-.81	-2.36
Placebo	-.06	-.19	.30	.017

Appendix E10 (cont.)

Analysis of the change in response accuracy to the go-signal on three tests of the HC task by the alcohol and placebo groups:

Source	SS	DF	MS	F	p
Between Subjects					
G	21.067	1	21.067	.878	.365
Error	335.972	14	23.998		
Within Subjects					
T	10.260	2	5.130	.492	.616
T X G	90.515	2	45.258	4.344	.023*
Error	291.698	28	10.418		

Mean change in response accuracy (%) on three tests of the HC task by the alcohol and placebo groups:

Group	Test			
	30 minutes	60 minutes	90 minutes	overall test mean
Alcohol	.36	-4.11	-2.03	-1.93
Placebo	-1.84	.39	-.35	-.60

Appendix E11

Analysis of variance of the change in number of inhibitions made at each stop-signal delay on the LC and HC tasks by the alcohol and placebo groups:

Source	SS	DF	MS	F	p
Between Subjects					
G	232.408	1	232.408	11.755	.004*
Error	276.783	14	19.770		
Within Subjects					
L	30.000	1	30.000	2.849	.114
L X G	8.533	1	8.533	.810	.383
Error	147.400	14	10.529		
T	1.587	2	.794	.287	.753
T X G	.029	2	.015	.005	.995
Error	77.517	28	2.768		
D	18.804	4	4.701	.404	.805
D X G	65.029	4	16.257	1.396	.247
Error	652.300	56	11.648		
L X T	5.788	2	2.894	1.265	.298
L X T X G	2.629	2	1.315	.575	.569
Error	64.050	28	2.288		
L X D	26.354	4	6.589	1.065	.383
L X D X G	20.863	4	5.216	.843	.504
Error	346.517	56	6.188		
T X D	12.058	8	1.507	.865	.549
T X D X G	5.533	8	.692	.397	.920
Error	195.275	112	1.744		
L X T X D	20.733	8	2.592	1.693	.108
L X T X D X G	4.725	8	.591	.386	.926
Error	171.408	112	1.530		

Appendix E12

Planned comparisons of the change in number of inhibitions made at stop-signal delays on the low-load change task for the alcohol group:

Source	SS	DF	MS	F	p
1 vs. 2,3,4,5	2628.125	1	2628.125	4.330	.076
Error	4248.875	7	606.982		
1,2 vs. 3,4,5	2812.500	1	2812.500	1.304	.291
Error	15095.500	7	2156.500		
1,2,3 vs. 4,5	4278.125	1	4278.125	1.948	.205
Error	15374.875	7	2196.411		

Planned comparisons of the change in number of inhibitions made at stop-signal delays on the high-load change task for the alcohol group:

Source	SS	DF	MS	F	p
1 vs. 2,3,4,5	128.000	1	128.00	.110	.750
Error	8144.000	7	1163.429		
1,2 vs. 3,4,5	630.125	1	630.125	.431	.532
Error	10232.875	7	1461.839		
1,2,3 vs. 4,5	72.000	1	72.000	.039	.850
Error	13006.000	7	1858.000		

Appendix E13

The change in inhibitions on both tasks under alcohol is shown in the table below. The results for the placebo group are shown for comparison.

Mean change in inhibitions as a function of stop-signal delay:

Group	Task	stop-signal delay (ms)				
		0	60	135	210	285
Alcohol	LC	-3.00	-1.83	-2.08	-1.38	-.67
	HC	-1.29	-.17	-1.42	-1.29	-.96
Placebo	LC	.04	-.08	-.5	.33	-.46
	HC	.42	-.17	.33	.54	-.63

The consistent decline in inhibitions as a function of stop-signal delays was evident under alcohol and placebo. The mean number of inhibitions (out of a possible 10 at each stop-signal delay) on each test is shown below.

Group	Task	stop-signal delay (ms)				
		0	60	135	210	285
Alcohol	LC	5.38	5.04	3.42	1.63	.46
	HC	6.96	7.08	5.46	4.08	1.67
Placebo	LC	7.79	6.92	4.75	2.83	1.29
	HC	8.92	7.96	6.96	4.79	2.63

Appendix F

Experimental Data

Alcohol Study 1

The raw data in Alcohol Study 1 is presented by subject.
Line 1 of the data presents subject characteristics and drinking habits in the following order:
1) subject number
2) group (2=placebo, 3=alcohol)
3) age (years)
4) weight (kg)
5) dose (ml/kg)
6) frequency (per week)
7) duration (hours)
8) rate (dose/duration)
9) estimated number of drinks from placebo manipulation check

Line 2 shows the response time to the go-signal (ms) on the low-load go-stop task on the baseline test and three treatment tests.

Line 3 shows the response time to the go-signal (ms) on the high-load go-stop task on the baseline test and three treatment tests.

Line 4 shows the subject's BAC (mg/dL) at 30, 50, 60, 70, 80, 90, 110 minutes following the onset of drinking.

Line 5 shows the number of inhibitions made at each of the four stop-signal delays (60, 135, 210, and 285ms) on the baseline test and three treatment tests of the low-load go-stop task.

Line 6 shows the number of inhibitions made at each of the four stop-signal delays (60, 135, 210, and 285ms) on the baseline test and three treatment tests of the high-load go-stop task.

Alcohol Group:

1 3 21 90.7 1.503 3 5 0.3006 3
380.61 371.39 394.94 375.26
399.28 423.85 426.58 427.78
35 50 65 60 70 70 75
12 11 5 1 12 10 2 0 10 11 8 0 11 6 3 1
12 12 8 3 11 12 8 0 11 10 7 5 11 10 6 0

2 3 20 70.3 2.425 2.5 4.5 0.538889 4.5

```
351.14 367.38 390.88 358.31
415.73 420.11 468.85 471.09
50 60 70 70 70 60 60
12 11 3 0 8 6 3 0 9 7 5 0 5 2 1 0
12 10 9 1 11 11 8 2 9 8 5 1 9 9 4 4

3 3 22 87.53 1.168 2 4 0.292 7
307.35 312.51 335.05 335.75
376.08 390.66 412.38 402.77
60 85 95 90 90 80 60
7 3 0 0 1 0 0 0 0 0 0 0 0 0 1 0
7 8 2 2 4 2 0 0 3 6 3 0 1 2 1 0

4 3 22 76.19 1.79 3 5 0.358 7
336.53 327.83 326.71 324.35
378.61 381.03 374.99 385.80
45 65 70 70 65 58 60
11 7 1 1 6 2 0 0 4 0 1 1 2 1 1 0
11 7 3 2 12 7 5 3 9 5 0 1 6 4 3 1

12 3 21 75.3 0.453 3 1.5 0.302 3.5
302.45 302.18 298.63 284.54
351.76 356.32 357.97 356.00
45 55 85 65 55 50 50
11 6 0 0 7 6 0 0 8 2 0 0 4 0 1 0
12 8 3 0 12 9 3 0 11 5 4 0 9 5 2 0

13 3 22 77.1 0.884 1 3.5 0.252571 3.5
316.16 306.08 307.05 313.30
355.32 362.34 366.52 360.12
40 65 72 75 70 70 65
12 8 0 0 11 4 0 0 9 3 0 0 8 7 1 0
12 10 5 0 12 8 2 0 12 9 2 0 12 7 2 0

15 3 22 84.81 1.407 0.25 2.5 0.5628 8
380.59 375.64 382.99 372.84
418.46 428.43 450.56 441.97
42 55 62 71 60 65 60
12 11 5 0 12 11 4 1 11 10 2 0 12 6 1 0
11 12 11 5 12 12 11 3 12 10 9 4 12 10 7 3

21 3 20 65.75 1.037 0.25 1.5 0.691333 1
421.05 499.66 492.28 520.10
```

531.18 569.32 579.72 504.62
50 65 60 67 65 68 70
12 12 11 9 12 12 9 7 12 11 10 7 12 10 11 7
12 11 11 12 11 12 11 9 12 12 12 3 6 9 6 4

Placebo Group:

6 2 21 86.2 0.99 0.5 3 0.33 1
337.99 334.33 323.14 318.27
418.15 393.99 401.23 414.37
10 0 0 0 0 0 0
5 6 1 1 4 2 0 1 1 2 0 0 10 0 0 0
7 5 2 0 7 1 1 2 9 4 2 1 4 3 2 0

7 2 20 92.9 0.917 2 3 0.305667 2.5
295.28 297.43 280.45 291.05
365.41 333.30 340.44 346.38
10 0 0 0 0 0 0
1 0 0 0 2 0 0 0 2 1 0 0 3 0 0 0
5 4 0 0 4 3 1 0 6 3 1 1 5 3 1 0

8 2 21 65.31 0.783 3 3 0.261 1
374.02 363.64 347.15 377.12
427.44 439.06 443.36 432.21
10 10 0 0 0 0 0
11 5 4 0 12 6 3 1 11 5 2 0 11 7 0 1
10 11 10 1 12 11 9 4 10 11 8 2 10 9 5 1

9 2 21 78.5 0.565 5 1.25 0.452 1
499.20 509.86 510.40 507.68
606.25 573.11 610.32 578.69
10 0 0 0 0 0 0
11 12 10 10 12 12 11 7 11 12 10 9 11 12 11 10
12 11 11 12 11 12 12 12 12 12 12 10 10 12 11 12

11 2 20 82.5 0.826 2 3 0.275333 3
310.01 318.76 313.31 319.50
352.92 363.51 365.85 371.20
15 10 10 0 0 0 0
9 3 3 0 11 7 0 1 12 7 0 0 9 3 0 0
12 6 0 0 12 11 1 0 11 6 2 1 11 8 2 1

```
14  2  21  71.2  1.676  1  7  0.239429  1
479.32  573.55  548.29  487.34
533.49  696.56  632.81  557.69
15  10  0  0  0  0  0
 8   6   6   3  12  11   9  11  12   9   9   5  12   8   5   4
 9  10   9   6  10  11  11  10   8  10  11   6   9  10   9   5

16  2  19  74.4  1.832  1  5  0.3664  2
394.49  379.67  371.62  367.60
452.58  446.11  450.23  454.67
10  10  0  0  0  0  0
 8  11   6   1  11   7   3   0  10   9   3   2   6   7   1   0
 9   9  11   5   9   8   8   0  10  11   9   5   8  11   9   2

20  2  21  77.6  1.32  1  4  0.33  5.5
321.43  322.91  315.76  318.77
369.52  364.68  360.12  367.53
10  10  0  0  0  0  0
12   7   2   0  12   5   1   0  12   9   2  0  12   7   2   0
12  12   4   0  12  12   4   1  12  11   3  1  12  11   4   2
```

Appendix F (cont.)

Experimental Data

Alcohol Study 2

The raw data in Alcohol Study 2 is presented by subject.
Line 1 of the data presents subject characteristics and drinking habits in the following order:
1) subject number
2) group (2=placebo, 3=alcohol)
3) age (years)
4) weight (kg)
5) dose (ml/kg)
6) frequency (per week)
7) duration (hours)
8) rate (dose/duration)
9) estimated number of drinks from placebo manipulation check

Line 2 shows the subject's BAC (mg/dL) at 30, 50, 60, 70, 80, 90, 110 minutes following the onset of drinking.

Line 3 shows the response time to the go-signal (ms) on the low-load change task on the baseline test and three treatment tests.

Line 4 shows the response time to the go-signal (ms) on the high-load change task on the baseline test and three treatment tests.

Line 5 shows the number of inhibitions made at each of the five stop-signal delays (0, 60, 135, 210, and 285ms) on the baseline test and three treatment tests of the low-load change task.

Line 6 shows the number of inhibitions made at each of the five stop-signal delays (0, 60, 135, 210, and 285ms) on the baseline test and three treatment tests of the high-load change task.

Line 7 shows RT2 inhibit (ms) on the baseline test and three treatment tests for the low-load change task.

Line 8 shows RT2 fail (ms) on the baseline test and three treatment tests for the low-load change task.

Line 9 shows RT2 inhibit (ms) on the baseline test and three treatment tests for the high-load change task.

Line 10 shows RT2 fail (ms) on the baseline and three treatment tests for the high-load change

task.

Alcohol Group:

4 3 19 83.9 0.846 2 3 0.282 2
60 80 78 76 75 68 60
380.83 405.73 393.04 403.15
495.11 495.27 504.09 550.94
10 8 7 6 4 9 8 6 4 1 9 10 6 4 2 9 9 8 4 2
10 10 9 7 5 8 10 10 6 2 9 10 7 6 2 10 5 8 4 2
469.66 488.68 431.03 451.88
420.07 599.68 528.61 539.11
478.09 509.43 475.15 494.50
494.67 543.33 641.64 627.44

5 3 19 73.7 1.156 2 2.5 0.4624 3.5
60 70 70 70 65 55 45
363.58 337.23 360.01 410.84
449.61 441.26 403.53 489.35
6 4 4 0 1 0 0 0 0 0 1 0 1 0 0 2 2 0 1 0
9 5 4 4 0 1 2 0 2 0 3 4 1 1 0 1 2 1 1 0
386.07 370.00 363.00 367.00
404.86 501.31 525.33 533.21
444.95 429.40 358.00 289.00
434.69 517.41 517.44 529.77

6 3 19 67.8 0.929 0.5 0.5 1.858 3.5
48 65 70 68 65 61 53
366.29 372.84 369.44 358.32
443.91 438.42 442.24 451.97
7 6 2 1 0 3 5 0 1 0 3 0 0 0 0 6 4 0 1 0
7 7 4 2 0 4 4 0 0 1 5 6 5 2 0 2 4 0 2 0
426.13 293.33 402.00 309.18
380.76 452.41 433.73 417.63
323.90 355.11 342.72 305.88
479.85 503.56 491.48 493.85

7 3 19 77.1 1.99 2 3.5 0.568571 4.5
32 51 65 65 60 50 45
412.34 454.34 465.13 478.49
484.86 539.13 550.37 504.19
9 8 5 2 0 2 3 4 2 0 1 2 2 0 0 4 3 2 0 0
7 7 7 4 2 10 6 7 6 4 3 8 0 4 0 6 4 5 1 1

395.38 438.36 494.40 493.67
458.41 494.43 595.70 533.38
423.15 452.55 483.23 430.41
480.45 501.79 542.93 428.54

11 3 23 74.4 0.715 0.5 3 0.238333 4.5
62 93 89 90 90 88 80
319.96 331.15 339.97 346.21
379.45 371.94 383.02 400.41
10 7 5 0 0 5 5 5 1 0 9 3 5 0 0 6 2 0 0 0
9 8 5 3 0 10 10 5 3 0 9 9 5 2 1 9 9 8 3 1
367.41 331.06 324.24 333.88
331.75 366.13 363.09 404.42
336.88 357.68 319.81 318.73
360.02 367.73 374.87 362.31

16 3 21 75.28 2.034 3.5 5 0.4068 6
65 78 83 85 90 88 80
423.47 380.20 429.73 431.26
531.25 492.72 531.36 541.77
9 7 6 6 0 6 6 6 0 0 6 6 3 2 0 6 9 3 3 0
9 5 7 7 3 8 9 9 7 3 9 8 8 9 2 9 10 7 9 5
456.68 422.39 388.06 424.62
491.62 458.00 470.67 491.93
470.10 441.92 430.72 396.85
526.82 486.57 533.23 549.78

19 3 22 63.2 1.348 7 5 0.2696 5
30 50 60 70 60 60 60
374.54 374.44 376.90 395.19
496.11 512.44 555.16 533.48
10 8 8 2 1 4 7 3 3 0 7 9 6 1 0 10 6 5 2 1
10 10 10 8 9 9 10 10 7 4 10 8 9 9 6 10 9 10 9 5
380.10 410.59 373.17 364.50
376.91 434.58 400.46 394.15
422.09 416.77 386.12 390.86
446.33 476.44 462.29 390.33

21 3 21 90.7 0.94 1 6 0.156667 8
58 65 60 60 60 60 55
421.44 412.37 430.08 433.22
446.75 491.94 470.50 474.84
6 7 7 7 3 5 5 3 2 3 8 10 5 5 0 8 7 9 3 2

7 6 9 5 0 8 7 3 3 1 4 8 7 1 0 9 8 6 1 0
450.13 406.28 360.39 387.69
535.88 428.24 405.94 370.50
331.30 397.82 361.45 354.04
418.79 471.12 433.79 402.87

Placebo Group:

12 2 20 56.69 2.104 2 5.5 0.382545 3
10 0 0 0 0 0 0
459.82 426.54 436.25 418.95
507.70 481.85 470.04 481.00
10 9 10 8 6 10 10 10 9 5 10 10 10 10 4 9 10 9 10 6
8 10 9 7 8 10 9 10 10 7 8 10 10 8 7 9 8 9 10 10
485.05 445.87 452.43 430.05
636.17 579.51 554.29 535.50
540.90 469.94 437.19 423.37
720.17 477.67 609.00 557.00

13 2 23 71.2 0.479 0.5 2 0.2395 1
15 10 0 0 0 0 0
348.93 340.87 367.42 348.42
427.47 393.41 409.76 410.82
6 4 0 0 0 7 5 0 0 0 6 3 1 0 0 8 2 0 0 0
7 2 2 0 1 8 4 1 1 0 6 4 0 1 0 9 3 1 0 0
439.10 467.82 464.20 424.89
383.92 396.26 385.13 398.95
405.00 391.79 497.00 509.46
454.94 386.51 397.83 439.32

14 2 19 72.8 0.937 1 4 0.23425 1
20 20 20 10 10 10 0
479.84 507.71 496.41 445.32
618.76 661.61 628.14 624.95
8 9 9 5 4 10 7 8 6 4 8 8 9 4 2 8 7 6 5 1
10 9 9 5 7 10 8 7 9 6 10 10 9 7 3 10 9 7 7 3
347.91 361.77 389.29 370.84
415.27 448.36 467.07 436.52
372.73 397.55 437.13 398.03
503.00 553.44 518.44 481.00

15 2 21 89.79 1.52 2 6 0.253333 3

10 10 10 0 0 0 0
429.85 407.14 395.95 405.47
538.57 518.73 499.94 496.07
5 7 7 2 4 2 6 1 0 1 7 3 1 1 1 7 6 4 2 1
9 10 7 6 5 10 10 7 4 3 10 10 8 3 2 9 9 9 3 4
422.88 348.40 398.58 341.50
468.00 380.17 428.47 443.73
466.03 470.84 407.91 421.16
523.56 444.40 370.36 494.00

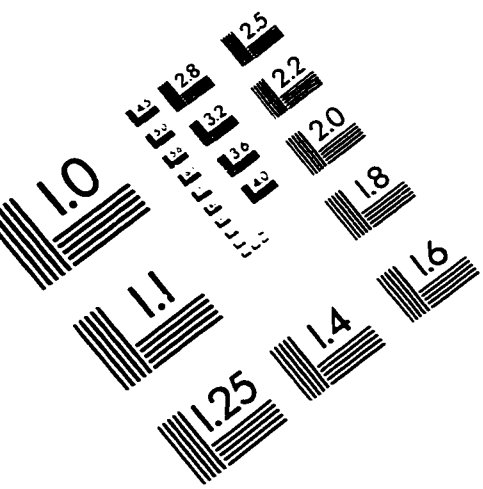
17 2 22 73.47 0.928 2 2 0.464 2
15 10 0 0 0 0 0
388.41 396.14 390.45 419.88
490.70 456.10 476.79 472.99
8 5 4 1 0 7 7 3 1 1 8 6 2 1 0 7 10 2 1 0
7 8 7 7 3 10 9 8 2 2 9 9 8 7 0 9 9 8 4 2
336.50 348.11 321.35 334.65
473.70 461.70 439.45 424.61
348.91 434.26 370.66 340.68
541.81 454.73 490.67 480.62

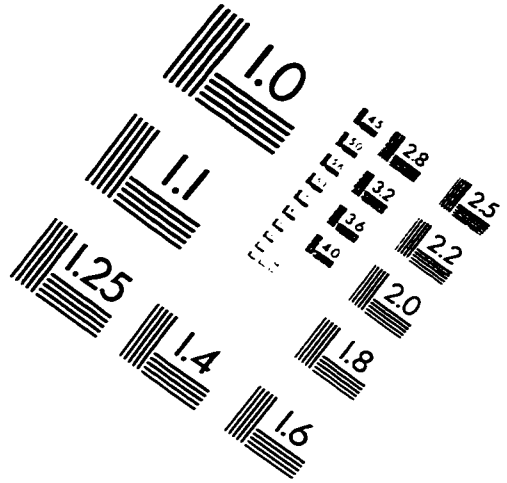
18 2 22 113.4 0.902 1 3 0.300667 3.5
10 0 0 0 0 0 0
380.57 388.60 424.75 430.10
454.38 502.27 522.72 507.74
10 9 5 2 0 7 6 7 3 1 9 8 4 5 1 8 8 8 3 2
9 10 9 5 1 9 8 7 8 2 9 5 8 5 2 9 8 7 5 2
362.96 359.79 365.93 385.55
451.61 489.14 492.17 518.67
367.86 386.62 411.28 407.37
504.44 542.13 559.00 532.54

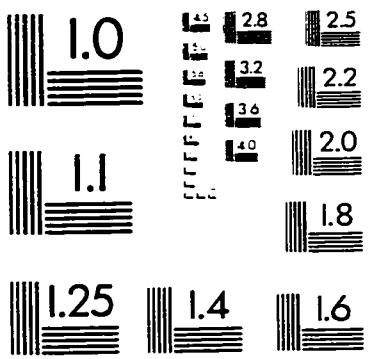
20 2 21 75.28 1.359 0.5 3 0.453 2
15 10 10 0 0 0 0
342.83 336.83 358.26 350.91
434.29 407.40 434.55 410.23
6 5 3 1 0 5 5 4 0 0 8 5 3 1 0 7 5 2 2 1
8 9 4 0 1 6 5 3 0 2 7 9 6 2 1 8 6 6 3 0
415.67 385.69 361.29 315.81
338.86 335.00 324.79 341.09
451.55 409.75 387.64 345.13
390.78 400.82 400.71 406.19

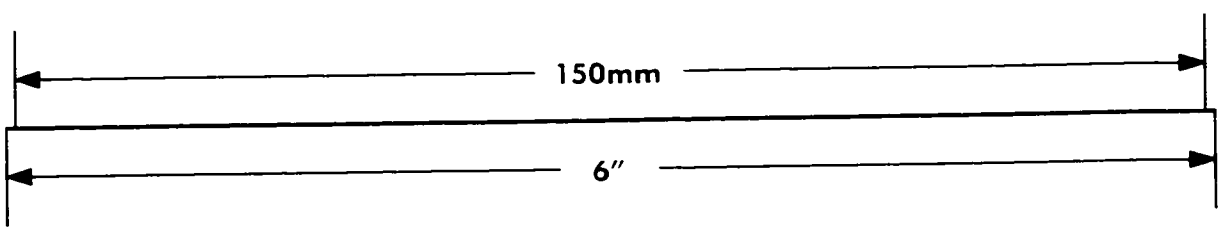
```
22  2  22  78  1.967  4  6.5  0.302615  2.5
0  10  10  0  0  0  0
314.62  332.83  353.14  342.42
368.14  385.58  387.44  382.73
 9   8   4   1   0  10  10  5   2   0  10  9   8   1   0  9   10  7   1   0
10   7   6   4   0  10   9   9   4   3   9  10  10  5   1  10  10   9   7   1
315.23  310.81  301.96  319.44
342.29  317.32  314.30  328.82
314.11  301.17  301.86  324.51
379.35  320.86  336.43  366.21
```

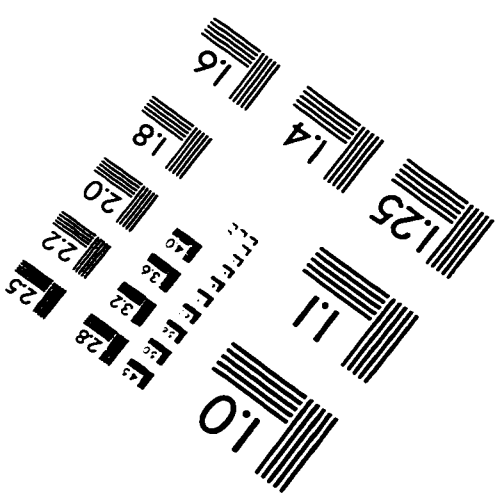
IMAGE EVALUATION
TEST TARGET (QA-3)

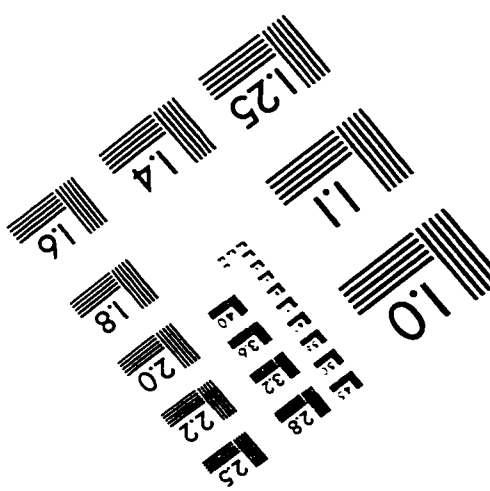












APPLIED IMAGE . Inc
1653 East Main Street
Rochester, NY 14609 USA
Phone: 716/482-0300
Fax: 716/288-5989