The Effects of Dehydration and Moderate Alcohol Consumption on Human Behaviour and Performance

Christopher Garry Irwin

Bachelor of Exercise Science (Griffith University), Bachelor of Education (Griffith University), Master of Nutrition & Dietetics (Griffith University)

School of Public Health and Research Centre for Health Practice Innovation
Griffith Health Institute
Griffith University, QLD, Australia

A thesis submitted in fulfilment of the requirements of the degree of
Doctor of Philosophy
September 2013

Statement of Originality

This thesis describes original research conducted by Christopher Garry Irwin in the School of Public Health at Griffith University. This work has not previously been submitted for a degree or diploma at any university. To the best of my knowledge and belief, this thesis contains no material previously published or written by another person except where due reference is made in the thesis itself.

Christopher Garry Irwin

Acknowledgements

Abstract

Human behaviour and performance are influenced by many factors. Alcohol consumption and dehydration are two factors that have individually been shown to have a detrimental impact on human behaviour and performance. Both of these factors have received significant scientific attention. Individuals may consume alcohol following a period of physical activity that causes fluid loss and results in dehydration. One could easily speculate that in combination, these factors may have a greater negative impact on performance and behaviour than in isolation. However, until now the combined effect of dehydration and alcohol consumption on human behaviour and performance has not been investigated. This thesis describes four main research studies in addition to four pilot investigations that were designed to examine the effects of dehydration and alcohol consumption on human behaviour and performance, specifically the cognitive skills related to driving a motor vehicle and driving-related risk taking behaviour.

In Research Study One, the hydration status of industrial workers was monitored over two work days before exploring typical post-work behaviours, attitudes and perceptions relating to alcohol consumption. Results from this study indicated that approximately one-third of workers were inadequately hydrated either at the beginning or end of work shifts. With respect to alcohol consumption, most of the workers believed drinking alcohol after work was acceptable, and a lack of consideration for hydration levels was indicated prior to consuming alcohol. The findings from this study suggest that some individuals are likely to consume alcohol following a period of physical activity that causes dehydration.

In Research Study Two, the effects of exercise-induced dehydration on alcohol pharmacokinetics and subjective ratings of alcohol's effects were examined. Dehydration was observed to have no impact on the pharmacokinetic response to a moderate dose of alcohol. However, dehydration did influence subjective ratings of confusion and intoxication when alcohol

was consumed and may influence driving-related risk taking behaviour, such as greater willingness to drive following alcohol consumption observed in dehydration trials.

Research Study Three investigated the effects of mild and moderate dehydration combined with moderate alcohol consumption on discrete cognitive functions assessed with a computerised test battery. Alcohol consumption caused deterioration in some cognitive performance measures and performance impairment was exacerbated when participants were dehydrated compared to being rehydrated prior to alcohol consumption. In contrast with the results from Research Study Two, subjective ratings of impairment and intoxication, and driving-related risk taking behaviour were not influenced by the interaction of alcohol and dehydration.

In the final Research Study, the effects of mild and moderate dehydration combined with moderate alcohol consumption on an applied cognitive task (simulated driving performance) were investigated. Whilst alcohol consumption had some influence on measures of vehicular control (standard deviation of lateral position), there was no observable interaction on driving performance with changes in hydration status that influenced performance. Similar to Research Study Three, no combined effects of hydration status and alcohol consumption were observed on subjective ratings of alcohol intoxication, driving impairment, or driving-related risk taking behaviour.

Collectively, the research presented in this thesis shows that dehydration may exacerbate alcohol induced impairment of some cognitive functions and behaviour. However, the interactive effect of dehydration and moderate doses of alcohol does not appear to be uniform across tasks or influential on performance tasks of an applied nature (i.e. driving performance). The influence of hydration status combined with various doses of alcohol consumption on human behaviour and performance requires further consideration.

Table of Contents

Glossary of Terms

~	Approximately		mg	Milligrams
°C	Degrees Celsius		mg/L	Milligrams per litre
%	Percentage		mg/100ml/hr	Milligrams per one hundred millilitres per hour
% v/v	Percent volume per volume		min	Minute(s)
ADH	Alcohol dehydrogenase		ml	Millilitres
BAC	Blood alcohol concentration		ml/kg BW	Millilitres per kilogram body weight
BrAC	Breath alcohol concentration		ml/kg BW/min	Millilitres per kilogram body weight per minute
BW	Body weight		ml/L	Millilitres per litre
CANTAB	Cambridge neuropsychological test automated battery		mm	Millimetre(s)
c.c.	Cubic centimetre(s)		mmol/L	Millimoles per litre
CHO	Carbohydrate		Na^+	Sodium
Cl^-	Chlorine		$[Na^+]$	Sodium ion concentration
$[Cl^-]$	Chloride ion concentration		NaCl	Sodium chloride
cm	Centimetre(s)		NHMRC	National Health and Medical Research Council
CNS	Central nervous system		Posm	Plasma osmolality
CRT	Choice reaction time		PET	Positron emission tomography
d	Day(s)		PPO	Peak sustained power output
D-R	Dose response		Pro	Protein
EF	Executive function		PV	Plasma volume
EFSA	European Food Safety Authority		RH	Relative humidity
F	Female		RPE	Rating of perceived exertion
fMRI	Functional magnetic resonance imaging		rpm	Revolutions per minute
g	Grams		RT	Reaction time
g/100ml	Grams per hundred millilitres		sMRI	Structural magnetic resonance imaging
g/kg	Grams per kilogram		SOC	Stockings of Cambridge
g/L	Grams per litre		SRT	Simple reaction time
g/ml	Grams per millilitre		STM	Short term memory
g/serve	Grams per serve		TBW	Total body water
GABA	Gamma-aminobutyric acid		TMT	Trail making test
hr	Hour(s)		TOL	Tower of London
kCal	Kilocalories		Ucol	Urine colour
kg	Kilograms		Uosm	Urine osmolarity
KJ	Kilojoules		U_{sg}	Urine specific gravity
L	Litres		VO_2	Volume of oxygen uptake
L/d	Litres per day		VO_{2max}	Maximum volume of oxygen uptake
LTM	Long term memory		vs.	Versus
M	Male		WCST	Wisconsin card sorting test
MEOS	Microsomal ethanol oxidising system		WHO	World Health Organization

List of Figures

List of Tables

Publications in Support of this Thesis

The research candidate has produced six publications from the research included in this thesis. The publications are co-authored with other researchers, and are original research papers. The contribution of the research candidate to each publication is outlined at the front of the relevant chapter. The details of these publications are listed in order as they appear in the thesis:

1. **Irwin C,** Desbrow B, Leveritt M. Development and effectiveness of a placebo beverage similar in sensory properties to an alcoholic beverage. *Journal of Alcohol and Drug Education*, 2011; 55(3):p15-22.

2. **Irwin C,** Shum D, Leveritt M, Desbrow B. Test-retest reliability of simulated driving performance: A pilot study. *Proceedings of the Seventh International Driving Symposium on Human Factors in Driver Assessment, Training and Vehicle Design*, 2013; Bolton Landing, New York:p285-291.

3. **Irwin C,** Leveritt M, Desbrow B. A hard earned thirst: Workplace hydration and attitudes regarding post-shift alcohol consumption. *Journal of Health, Safety and Environment*, 2013; 29(1):p51-67.

4. **Irwin C,** Goodwin A, Leveritt M, Davey AK, Desbrow B. Alcohol pharmacokinetics and risk-taking behaviour following exercise-induced dehydration. *Pharmacology Biochemistry and Behavior*, 2012; 101(4): p609-616.

5. **Irwin C,** Leveritt M, Shum D, Desbrow B. The effects of dehydration, moderate alcohol consumption and rehydration on cognitive functions. *Alcohol*, 2013; 47(3): p203-213.

6. **Irwin C,** Shum D, Leveritt M, Desbrow B. Mild to moderate dehydration combined with moderate alcohol consumption has no influence on simulated driving performance. *Traffic Injury Prevention*, 2013; (In Press).

In addition, the research within this thesis has been presented at four international conferences, two national conferences and two local conferences.

1. **Irwin C,** Shum D, Leveritt M, Desbrow B. Test-retest reliability of simulated driving performance: A pilot study (Poster). *Seventh International Driving Symposium on Human Factors in Driver Assessment, Training and Vehicle Design*, Bolton Landing, New York, USA, 2013.

2. **Irwin C**, Goodwin A, Leveritt M, Davey A, Desbrow B. The effect of dehydration on the blood and breath alcohol responses to moderate alcohol consumption (Oral). *International Congress of Dietetics*, Sydney, Australia, 2012.

3. **Irwin C**, Goodwin A, Leveritt M, Davey A & Desbrow B. Exercise-induced dehydration has no effect on alcohol pharmacokinetics but influences willingness to drive (Poster). *American College of Sports Medicine Conference*, San Francisco, USA, 2012.

4. **Irwin C,** Desbrow B, Leveritt M. Development and effectiveness of a placebo beverage similar in sensory properties to an alcoholic beverage (Interactive Poster). *Griffith University Health and Medical Research Conference*, Gold Coast, Australia, 2011.

5. **Irwin C**, Goodwin A, Leveritt M, Davey A, Desbrow B. The effect of exercise-induced dehydration on alcohol pharmacokinetics and subjective ratings of impairment following moderate alcohol consumption (Poster). *Sports Dietitians Australia Conference*, Melbourne, Australia, 2011.

6. **Irwin C**, Leveritt, M, Shum D, Desbrow B. The effect of dehydration and moderate alcohol consumption on cognitive function and reaction times (Oral). *16th Congress of the European College of Sports Science*, Liverpool, United Kingdom, 2011.

7. **Irwin C**, Leveritt, M, Shum D, Desbrow B. The effect of dehydration and moderate alcohol consumption on cognitive function and reaction times (Oral). *2nd Sport and Alcohol Conference: Finding the Balance*, Auckland, New Zealand, 2011.

8. **Irwin C**, Leveritt, M, Shum D, Desbrow B. The effect of dehydration and moderate alcohol consumption on cognitive function and reaction times (Poster). *Griffith University Health and Medical Research Conference*, Gold Coast, Australia, 2010.

Chapter One: Introduction

1.1 Background and Context

Alcohol is one of the most commonly consumed psychoactive substances in the world. It is a naturally occurring preservative and as a consequence it is tied up in religious belief and behaviour. However, purposeful production and consumption of alcohol dates back to ancient civilisations, and has been considered as pre-dating cultures of religious faith. Many factors contribute to the popularity of alcohol consumption, such as its legal availability and association with social practices (National Health and Medical Research Council, 2009). Alcohol is very much a part of Australian culture, with consumption regarded as normal, sociable and sometimes even *expected* (NSW Office of Drug Policy, 2003).

The circumstances leading to alcohol consumption may be an indirect influence of a specific social atmosphere, or may be part of an individual's customary routine. For many, alcoholic beverages are chosen as a means to quench thirst following a period of physical exertion or activity. It is common to see tradesmen having a drink at the pub after a day of physical work, or sporting participants celebrating with alcohol after a game. Currently, there is a lack of understanding regarding the attitudes, perceptions and behaviours of regular drinkers that consume alcohol following a period of physical exertion or activity (Janes & Ames, 1989).

Physical exertion generates body heat, increases body temperature and subsequently results in fluid loss through sweating. Under conditions where fluid loss exceeds intake, dehydration occurs. Given that many people do not voluntarily consume sufficient volumes of water (Hubbard et al., 1984), individuals who drink alcohol after being physically active are possibly doing so in a dehydrated state.

Alcohol affects the central nervous system (CNS) and influences brain function and performance (Eckardt et al., 1998). The detrimental effect of acute alcohol consumption on a range of cognitive performance tasks have been well documented (Fillmore, 2007). Alcohol impairs judgement and physical abilities as evidenced by performance impairment on discrete tasks (Ogden & Moskowitz, 2004) as well as applied situations such as driving a motor vehicle (Moskowitz & Robinson, 1988; Moskowitz & Fiorentino, 2000). Alcohol consumption has also been associated with increased risk-taking behaviour (Lane et al., 2004), which has obvious consequences associated with injury and harm (i.e. motor vehicle accidents and fatalities). These events are a major public health issue in Australia and are often the topic of serious debate regarding statutory alcohol driving limits, drinking age recommendations and alcohol education programs. Interestingly, studies examining the impact of dehydration on cognitive function have also indicated performance decrements as a result of fluid loss induced through exercise (Grandjean & Grandjean, 2007; Lieberman, 2007). It is generally accepted that reductions in cognitive performance are proportionate to the degree of dehydration and that cognitive impairment becomes detectable with fluid deficits of >2% body mass loss (Lieberman, 2007; Shirreffs, 2009).

At present, studies have only considered the individual or independent effects of dehydration and alcohol consumption on cognitive performance. No literature currently exists describing the effects of dehydration and moderate alcohol consumption in combination, attitudes towards drinking alcohol following fluid loss, or the subsequent influence of dehydration and alcohol consumption on cognitive performance and risk-taking behaviour. However, many people consume alcoholic beverages following activities that are physically demanding, where fluid loss through sweating is expected. Sweat production reduces the total body water content of an individual (Sawka et al., 2007). The effect of this total body water shift on the physiological interaction with alcohol and subsequent metabolism of the substance is currently unclear.

Furthermore, the consumption of alcohol under conditions where dehydration occurs may cause further deterioration in cognitive function and influence risk taking behaviour. Ultimately, this may influence an individual's ability to carry out everyday tasks such as driving a motor vehicle or operating machinery.

1.2 Research Aims

The overall objective of this thesis is to explore the effects of mild and moderate dehydration combined with moderate alcohol consumption on human performance and behaviour. This thesis incorporates four main aims:

1. Determine the hydration status of a population group likely to be involved in daily physical exertion that causes dehydration (i.e. industrial/construction workers) and explore the typical post-work behaviours, attitudes and perceptions toward alcohol consumption.

2. Investigate the effects of dehydration on alcohol pharmacokinetics and subjective ratings of alcohol intoxication, impairment and driving-related risk taking behaviour.

3. Examine the effects of dehydration, moderate alcohol consumption, and rehydration on a range of cognitive functions using discrete cognitive tasks (i.e. reaction time, executive function and cognitive inhibition).

4. Examine the effect of dehydration, moderate alcohol consumption, and rehydration on cognitive performance associated with applied tasks such as driving a motor vehicle.

These four aims have been met by four specific research studies, with each of the studies presented as a separate chapter in this thesis. Four pilot investigations were also completed as part of the overall thesis, to improve methodological accuracy, validity, and reliability within the main research studies of this thesis. The aim of each pilot study was to:

3

1. Develop a placebo beverage that was similar in sensory properties to that of an alcohol-containing beverage, allowing it to be used to examine the expectancy effects of alcohol.

2. Examine the accuracy and reliability of breath alcohol analysis using a handheld police grade breathalyser under conditions of exercise-induced dehydration. Breath alcohol analysis was to be used in subsequent Research Studies (Chapters Six, Seven and Eight) to determine intoxication levels.

3. Determine the test-retest reliability of assessment tasks from the Cambridge Neuropsychological Test Automated Battery (CANTAB). A specific group of tasks from the CANTAB were to be used in one of the main research investigations of this thesis. Test-retest reliability data from these tasks would provide greater confidence in the interpretation of results in Research Study Three (Chapter Seven) where the instrument was employed.

4. Determine the test-retest reliability of performance measures collected on a computerised driving simulator. A driving scenario was developed for use in the final main study of this thesis. Test-retest reliability data of assessment measures from the driving simulator scenario would provide greater confidence in the interpretation of results from Research Study Four (Chapter Eight) where the driving simulator task was used.

1.3 Structure of Thesis

Chapter Two of this thesis provides an extensive review of the literature detailing the current state of knowledge regarding the effects of hydration status and alcohol consumption on cognitive performance and human behaviour, highlighting areas in need of further study. These areas formed the background to the primary research questions addressed in subsequent thesis chapters. Chapter Three provides a research framework outlining the approach taken towards the

Research Studies as a collective. Chapter Four includes four separate methodological investigations (Pilot Studies One to Four), where development of specific research tools and the validity and reliability of these were determined, as outlined earlier. Chapter Five reports the findings of an investigation related specifically to the first aim of this thesis, that is, determining the hydration status of industrial workers and exploring post-work behaviours, attitudes and perceptions towards alcohol consumption. Chapter Six relates to the second aim of this thesis, investigating the effects of dehydration on alcohol pharmacokinetics and subjective ratings of alcohol intoxication, impairment and driving-related risk taking behaviour. Chapter Seven relates to thesis aim three and examines the effects of dehydration, moderate alcohol consumption and rehydration on a range of cognitive functions assessed with specific tasks from the CANTAB. Chapter Eight relates directly to the fourth aim of the thesis and examines the effect of dehydration, moderate alcohol consumption and rehydration on simulated driving performance. The thesis concludes with a general discussion of the research findings from the entire body of research undertaken and draws together the conclusions and recommendations therein (Chapter Nine).

Chapter Two: Review of the Literature

2.1 Preface

This chapter explores previous research examining dehydration and alcohol consumption and their impact on human behaviour and cognitive performance. The researcher is currently unaware of any studies investigating the effects of dehydration and alcohol consumption in combination. Therefore, these components have been reviewed separately in this chapter.

The literature review firstly provides an introduction to the role and requirements of fluid, how hydration status is determined and the physiological and cognitive effects associated with dehydration. Peer-reviewed journal articles were identified through bibliographic databases including PubMed, ISI Web of Knowledge, Proquest, and Google Scholar using a combination of search terms including fluid, hydration, dehydration, hypohydration, cognitive performance, and cognitive function. Cross matching of citation reference lists and forward citation searches were also completed to ensure all relevant articles were sourced.

Secondly, literature investigating the effects of 'low' and 'moderate' alcohol consumption on cognitive function and risk taking behaviour was reviewed. To simplify the reading of this literature review, the term 'alcohol' has been used in reference to ethyl alcohol or ethanol, the psychoactive substance in alcoholic beverages. This section begins with a brief discussion on the social context of alcohol use in Australia before exploring the fate of alcohol in the human body and the physiological and behavioural effects of alcohol consumption. Focus has been given to the effects of alcohol on cognitive performance, specifically to cognitive tasks involving mental chronometry (i.e. reaction time) and executive functions (i.e. attention, planning, response inhibition); cognitive skills likely to be involved in driving a motor vehicle. Peer-reviewed journal articles were identified using similar methods as previously described via a combination of search terms including alcohol,

cognitive performance, cognitive function, physical activity, risk taking, human behaviour, driving, and simulated driving performance.

One of the features about the area of alcohol research is the enormity of published research that exists. It is difficult to summarise the literature describing the effects of alcohol, given that many investigations have employed vastly different experimental designs, particularly around alcohol administration (e.g. dose, concentration, beverage type, consumption time, prandial conditions). In addition, investigators often have different definitions of acute alcohol consumption (e.g. light/low, moderate, and heavy/high) and describe these levels using different measures (e.g. g/kg, no. of drinks, blood or breath alcohol concentration). For the purpose of this literature review, the term 'moderate' alcohol intake refers to levels associated with blood (BAC) or breath (BrAC) alcohol concentrations between 0.04% and 0.10%. It follows that 'low' alcohol refers to levels below 0.04% and 'high' refers to levels above 0.10%. These values are described in the literature as the critical points where exponential increases in the risk of being involved in a motor vehicle accident under the influence of alcohol occur (Blomberg et al., 2005).

2.1.1 Measuring Cognitive Function

Cognitive psychology is a sub-discipline of psychology that endeavours to explain how people acquire, store, transform, use and communicate information (Neisser, 1967). In particular, cognitive psychology encompasses everyday processes such as attention, memory, perception, recognition, recall, reasoning, problem solving and decision making (Galotti, 2013). Two categories of behaviour assessment are typically used to measure changes in cognitive function; tests of cognitive performance and self-report based questionnaires. However, one of the challenges with investigating factors that may influence cognitive function is employing appropriate assessment tasks with the sensitivity to detect changes in cognitive state, particularly where only subtle perturbations in performance may exist.

There are many different tests available that can be used to assess cognitive function. Acute alcohol consumption has been associated with impairment on a broad range of cognitive performance measures, including reaction time, visual and auditory acuity, hand-eye coordination, gross body movements, memory, arithmetic tasks, mental tasks and applied tasks such as driving a motor vehicle or flying aircraft (Moskowitz & Fiorentino, 2000; Fillmore, 2007). On the other hand, definitive information is not available on cognitive functions that are especially sensitive to dehydration (Lieberman, 2012). Domains of cognitive performance that appear to be more consistently degraded by dehydration include vigilance, short-term memory, reasoning, and hand-eye coordination (Lieberman, 2012).

Mood and symptom based subjective questionnaires offer an alternate measure of function and often provide more valuable data than performance based assessments. These measures indicate individuals' perceptions of impairment to stressors, which may help to explain objective changes in performance. Changes in alertness, coordination, confusion, competence and fatigue are some of the potential symptoms of both alcohol consumption and dehydration, which can easily be measured using questionnaires (Ekman et al., 1963; Sher, 1985; Lex et al., 1988; Cian et al., 2001; Shirreffs et al., 2004; Szinnai et al., 2005).

Given the lack of definitive information for tasks that are particularly sensitive to dehydration, the following literature review includes a review of all available literature exploring the effects of dehydration on any cognitive performance task. Due to the large amount of literature examining the effects of alcohol consumption across a range of cognitive domains, the review has been narrowed to tasks involving assessment of reaction time, executive functions (including response inhibition) and driving performance.

2.2 Fluid

2.2.1 Roles and Requirements of Fluid

2.2.2 Measuring Hydration Status

2.2.3 Mechanistic Action of Dehydration on Cognitive Impairment

2.2.4 Effects of Dehydration on Cognitive Performance

2.2.4.1 Level of Dehydration

2.2.4.2 Method of Dehydration

2.2.4.3 Dehydration and Discrete Cognitive Tasks

2.2.4.4 Dehydration and Driving Performance

2.2.5 Summary

2.2.1 Roles and Requirements of Fluid

Water is a vital nutrient for life and a multifunctional constituent of the human body (Jequier & Constant, 2010). Maintenance of Total Body Water (TBW) balance is essential for practically all functions of the body. In particular, it plays an important role in thermoregulation (European Food Safety Authority (EFSA), 2010). Water accounts for approximately 50-70% of body weight (BW), however this volume varies with body composition (lean and fat mass) and is therefore generally greater in males (60-70% BW) compared to females (50-55% BW) (Oppliger & Bartok, 2002; Jequier & Constant, 2010).

Water loss occurs naturally in humans as part of daily living. The majority of daily losses occur through urine (~1-2 litres), faeces (~200ml), the respiratory work of the lungs (~250-400ml), and via the skin (~450-500ml) (Maughan, 2003; Jequier & Constant, 2010). In general, this equates to about 2-3 litres per day (L/d) for a sedentary adult (Jequier & Constant, 2010). However, these amounts vary greatly between individuals and are influenced by many factors such as dietary intake, environmental conditions and physical activity levels. Based on approximate daily losses, the general recommendations for daily water consumption by Australian adults (aged >19 years)

set by the National Health and Medical Research Council (NHMRC) are approximately 3.4 L/d for men and 2.8 L/d for women. The majority of water consumption (75%) is obtained from direct intake of fluids, with the remainder consumed within foods (National Health and Medical Research Council, 2005). Individuals exposed to extremely hot climates, and those who are physically active require higher amounts of fluid to counteract increased losses.

Fluid and electrolyte homeostasis is well regulated in humans. Water losses are usually corrected over a 24hr period provided adequate fluid consumption occurs (Grandjean & Campbell, 2004; Jequier & Constant, 2010). Under normal conditions (modest temperature and activity levels), body water volume fluctuates by less than 1% each day (Benelam & Wyness, 2010). However, fluid losses can be exacerbated, especially under conditions of applied physiological stress (i.e. physical exertion, exercise and heat exposure). These conditions can induce increased sweating rates, which often result in fluid losses that exceed voluntary consumption. When fluid losses exceed gains, this leads to body water deficit, also known as dehydration (European Food Safety Authority, 2010).

2.2.2 Measuring Hydration Status

Total body water turnover is complex and currently there is no general agreement on the most effective method of assessing an individual's hydration status at a given point in time (Maughan, Shirreffs, & Leiper, 2007). There are, however, a number of techniques commonly used for the assessment of hydration status, which involve either whole body, haematologic, urinary, or sensory measurements (Armstrong et al., 1994; Shirreffs, 2000; Oppliger & Bartok, 2002; Armstrong, 2005, 2007; Maughan, Shirreffs, & Leiper, 2007; Jequier & Constant, 2010).

Direct measures of TBW through isotope dilution techniques have generally been regarded as the "gold standard" of hydration measurement (Armstrong, 2007). Primarily, this involves oral or intravenous administration of a tracer substance (usually a solution containing a stable isotope of

hydrogen or oxygen) and then sampling of body fluid or expired air three to four hours later to determine tracer concentration and allow subsequent calculations of TBW (Armstrong, 2005). However, the validity of this technique has come under scrutiny due to its low applicability and impracticality during daily activities where body fluids are rarely stable (Armstrong, 2007). In addition, the technique is expensive, labour intensive and has a potentially greater likelihood of adverse events associated with the use of large doses of tracer substance (Bartoli et al., 1993). As a result the technique is rarely employed in research studies as a primary measure of hydration status.

Plasma osmolality (P_{osm}) and plasma volume (PV) changes are widely used as haematological indices of hydration (Armstrong, 2005). Plasma osmolality is a measure of the solute concentration in blood and direct measurements are performed with either a freezing point depression osmometer or vapour pressure depression osmometer (Erstad, 2003). Generally, increases in osmolality are seen as levels of dehydration increase (Shirreffs, 2000). However, the use of P_{osm} as a valid measure of whole body hydration has come under question, with fluctuating levels of TBW, fluid intake, fluid loss, and the variability of fluid in different compartments reducing the validity of this measure under all conditions and in all settings (Armstrong, 2007). In addition, the assessment methods required to determine P_{osm} involve blood sampling, require more technical expertise, and are more intrusive than other measures (Armstrong, 2007). Plasma volume changes are calculated from haemoglobin and haematocrit concentrations. Dehydration causes protein-free filtrate to leave the bloodstream and results in reduced PV. This is reflected by an increase in the concentration of protein in the remaining plasma (Dill & Costill, 1974). However, the relative changes in plasma volume associated with exercise induced dehydration appear to be small, with suggestions that plasma volume is defended in an attempt to maintain cardiovascular stability until a certain degree of body water loss has occurred (Shirreffs, 2000). Furthermore, like

measures of P_{osm} this technique requires some expertise, is invasive and is susceptible to subtle changes such as posture during collection phases (Harrison, 1985; Shirreffs, 2000).

Urinary based measurements such as urine osmolality (U_{osm}) and urine specific gravity (U_{sg}) are also extensively used as hydration status markers (Shirreffs, 2000). The specific gravity of urine represents the concentration of excreted solutes in the urine and refers to the density of a sample compared to pure water (Armstrong, 2005). In humans, normal urine specimens have U_{sg} values ranging from 1.013 to 1.029 g/ml, with values of ≤ 1.020 g/ml indicative of being euhydrated (Sawka et al., 2007), U_{sg} values exceeding 1.020 g/ml indicating dehydration (Armstrong et al., 2010), and values between 1.001 to 1.012 g/ml typically seen in hyper-hydrated states (Armstrong et al., 1994). Specific gravity can be measured quickly and accurately, with relatively little expense or expertise required, and is thought to reflect an individual's true hydration level (Armstrong, 2007). However, urine indices of hydration status may be limited in identifying changes in hydration status during periods of rapid body fluid turnover with less sensitive and delayed responses to fluid losses reported than other measures (Shirreffs, 2000; Popowski et al., 2001).

Urine colour (U_{col}) is a simple urinalysis measure commonly used to determine hydration status (Armstrong et al., 1994). Generally, it involves the collection of a urine sample and rating of it's colour against an eight point scale that is directly proportional to level of dehydration (Armstrong et al., 1994; Armstrong et al., 1998; Armstrong, 2005). Armstrong and colleagues (1998) found that U_{col} tracked changes in body water as effectively as (or better than) U_{osm}, U_{sg}, urine volume, and P_{osm} and concluded that U_{col} is a valid index of hydration status. However, in an earlier study Armstrong et al., (1994) noted that while U_{col} is an acceptable estimate of hydration status in industrial or field settings, it should not be used as the principal measure in laboratories where greater precision and accuracy are required. In addition, a more recent publication by Armstrong (2005) highlights that urinary measures of hydration status such as U_{col} are not infallible and can

often be poor indicators of hydration status because it mirrors the volume of fluid consumed rather than water retained in the body when large boluses are consumed.

Measuring hydration status based on acute changes in body weight is a method often used in investigations examining the acute effects and responses to dehydration (Kavouras, 2002). When food and fluid intake is controlled, the body mass differences measured pre and post hydration/dehydration intervention can safely be assumed as water loss or gain. This approach assumes that 1ml of sweat loss represents a 1g loss in body weight (Sawka et al., 2007). However, Maughan, Shirreffs, & Leiper (2007) have reported that the estimation of hydration status from changes in body weight are subject to several sources of error and may give rise to misleading results. The authors expressed concern that total mass loss results from several indices including respiratory water loss and substrate oxidation, but that net mass gain also occurs through fat oxidation and increased water availability as endogenous carbohydrate stores are oxidised. In addition, volumes of water content in the bladder and gastrointestinal tract that are not involved in hydration, but influence overall body mass, are difficult to measure and are often misrepresented as a hydration indicator when gross body mass measurements are used (Maughan, Shirreffs, & Leiper, 2007). In an effort to improve the validity of using body weight measures as an indicator of hydration status, Armstrong (2005) suggests that body weight measurements made at intervals of four hours or more should be corrected for factors such as substrate oxidation and respiratory water loss in order to establish the net effects of fluid balance. However, overall this method is still widely utilised and appropriate in research settings where change in hydration status is monitored and serial measurements are collected. Under these conditions, measuring body mass change requires little time and expertise, is of little expense, and is a safe and non-intrusive hydration assessment method, providing an accurate indication of hydration status in real time (Armstrong, 2007).

13

In summary, there are various techniques available to assess individual hydration status. Some of these methods are cost prohibitive, involve invasive procedures or are inappropriate for use in laboratories where greater precision and accuracy are required. Other simple measures, such as changes in body weight and U_{sg} appear to be accurate and reliable, cost effective, time efficient, require relatively little technical expertise and have a low likelihood of adverse events. These are measures that can also easily be adapted into occupational environments in order to monitor the hydration status of workers throughout the work shift.

2.2.3 Mechanistic Action of Dehydration on Cognitive Impairment

Several mechanistic theories have been proposed for the cognitive impairment observed with dehydration (Wilson & Morley, 2003; Maughan, Shirreffs, & Watson, 2007). Based on current research, it is hypothesised that these occur through an integration of hormonal and cellular responses, in reply to the fluid shifts caused by dehydration (Wilson & Morley, 2003). This may directly influence the CNS through changes in neuronal function and neurotransmission (Maughan, Shirreffs, & Watson, 2007).

Recent studies by Kempton et al., (2009; 2011) examined the effects of dehydration on brain structure, function and blood flow using structural (sMRI) and functional (fMRI) magnetic resonance imaging, and arterial spin labelling techniques. Participants underwent an exercise induced dehydration protocol with (1.64% BW loss) or without (0.53% BW loss) an additional thermal component. Cognitive performance was measured using an executive function task, with fMRI performed simultaneously, pre and post dehydration. The authors found that exercise induced dehydration caused subtle decreases in brain volume with secondary increases in ventricular volume. No differences were reported in cognitive task performance between conditions. However, thermal dehydration required a higher level of neuronal activity for equal performance measures, suggesting an inefficient use of brain metabolic activity. One could

speculate that at higher levels of dehydration or using alternative cognitive tasks, brain metabolic resources may diminish significantly and neuronal activity may not be able to compensate, which could result in a deterioration of cognitive performance. These latest findings provide further insight into the possible mechanisms responsible for cognitive performance deficits observed with dehydration. Ultimately, this work suggests that dehydration may adversely impact cognitive performance through structural and functional brain alterations. Further evidence is required to determine the exact mechanisms that cause dehydration-induced cognitive impairment. However, regardless of the mechanism, the effects of dehydration on cognitive function are evident.

2.2.4 Effects of Dehydration on Cognitive Performance

A number of publications (*n*=40) investigating the impact of acute dehydration on cognitive performance are available. Table 2.2a provides a summary of results from this research with studies categorised based on the method of dehydration.

Table 2.2a. Summary of studies investigating dehydration and cognitive performance

Dehydration Intervention	No. of Studies	Total Subjects	Dehydration Level (%BW loss)	Studies Reporting Impairment * (%)	Studies Reporting Improvement * (%)
Exercise	9	93 M, 57 F	0.53 – 4.1	5 (56)	2 (22)
Passive Heat Exposure	4	56 M	2.5 – 4.0	3 (75)	0 (0)
Exercise + Heat	16	169 M, 19 F	0.2 – 4.3	10 (63)	5 (31)
Exercise + Diuretics	2	26M, 25 F	1.39 – 1.59	1 (50)	0 (0)
Extended Fluid Deprivation	6	36 M, 46 F	1.45 – 2.7	4 (67)	0 (0)
Extended Fluid Deprivation + Exercise	2	42 M	1.2 – 2.5	1 (75)	0 (0)
Bowel Preparation	1	23 M, 15 F	2.6	0 (0)	0 (0)
TOTAL	**40**	**445 M, 162 F**	**0.2 – 4.3**	**24 (60)**	**7 (18)**

* Studies reporting significant impairment or improvement in cognitive performance on at least one examined task. M = Male, F = Female, BW = Body Weight.

The majority of studies have used a controlled exercise intervention in their methods to induce dehydration (*n*=29). A small number of other studies (*n*=11) have employed alternative methods to induce dehydration such as fluid deprivation over an extended period of 12-37 hours (Neave et

al., 2001; Shirreffs et al., 2004; Szinnai et al., 2005; Petri et al., 2006; Pross et al., 2012; Smith et al., 2012), passive heat exposure (Epstein et al., 1980; Cian et al., 2000; Cian et al., 2001; Ely et al., 2013), and bowel preparation techniques (Ackland et al., 2008). As these studies have not employed methods involving physical exertion; the intervention to induce dehydration within this thesis, they will not be discussed further in the literature review. A detailed description of original research studies employing exercise as a dehydration method is provided in Table 2.2b, with individual variations in methodology indicated including the cognitive tasks utilised, timing of tests and specific conditions relevant to the procedures of the study.

Table 2.2b. Studies investigating the effects of exercise-induced dehydration on cognitive performance (*n*=29)

Study	Subjects (*n*)	Dehydration Intervention	Dehydration Level	Cognitive Task	Time of Test	Conditions	Impairment with Dehydration	Findings
Exercise Induced Dehydration								
Cian, et al., (2000)	8 M	Treadmill run at 60% VO$_{2max}$ for ~2hrs	2.8% BW	LTM, CRT, Perceptive discrimination, STM, Unstable tracking	30min post dehydration and 15min post arm crank exercise	3 days prior to testing subjects refrained from strenuous exercise and drank 2L water/day. Standardised bkfast on morning of trial.	Yes	Both dehydration conditions impaired cognitive ability (perceptive discrimination, psycho-motor skills, STM) with no differences between trials. Tracking performance was impaired following arm crank exercise in dehydration conditions only. LTM impaired in both control and dehydration conditions.
Cian, et al., (2001)	7 M	Treadmill run for 2hrs at 65% VO$_{2max}$ (Tcore under 39 degrees)	2.8% BW	LTM, Perceptive discrimination, RT, STM, Unstable tracking, Subjective questionnaire	30min post dehydration	3 days prior to testing subjects refrained from strenuous exercise and drank 2L water/day. Standardised bkfast on morning of trial. In F trials subjects drank solutions containing 50g/L glucose + 1.34g/L NaCl + 1.5ml/L sugar-free green lemon flavour in volume of water equiv. to 100% BW loss. In NF and C trials subjects given 50g/L glucose in 100ml water.	Yes	Heat stress and exercise have negative effect on cognition, with no difference between the two dehydration methods. Longer response times but no effect on errors, STM affected but no effect on LTM. 3.5hrs after dehydration no longer had any effect on STM but subjects felt increasingly tired. LTM impaired in both control and dehydration compared to rehydration.
Grego, et al., (2005)	8 M	3hrs cycling at 60% VO$_{2max}$ with or without fluid	4.1% BW = NF, 2.2% BW = FC	Perceptual response - CFF test, Map recognition - map orienteering with projected slide	Before, During (every 20min) and After Exercise	Maintained same dietary and fluid intake on day prior to trials. Hydration trial = 400ml mineral water immediately prior to and 200ml at 20min intervals during cycle task. Cognitive tests completed in last 5min of each 20min block during exercise and within 5min post exercise.	Yes	No sig. effect of test duration on cognitive performance observed in control group. Sig. but differentiated effect of exercise duration found for both tasks in experimental group without any interaction effect with hydration status.
Edwards, et al., (2007)	11 M	45min cycle at 90% VT & 45min soccer match	0.73% BW = FC, 2.14% BW = MR, 2.4% BW = NF	Mental concentration test	Post YYIRT	Fasted 2.5hrs. Bkfast, MT and fluid consumed at will prior to 2.5hr fast. 5ml/kg BW water consumed 2hrs prior to test.	No	No sig differences in mental concentration across the 3 different conditions. Performance in YYIRT sig impaired with dehydration conditions.
D'Anci, et al., (Study 1) (2009)	16 M & 15 F	60min high intensity rowing or 75min of lacrosse drills	1.8% BW	STM, SRT, CRT, Map Planning, Mathematical Addition, Vigilance, Visual Perception	After Exercise	Abstinence from alcohol for 24hrs, caffeine for 6hrs and tobacco for 2hrs prior to testing. 1L of water received on test day to be consumed prior to testing.	Yes	No sig. effects of hydration status on digit span performance, SRT, CRT, map planning or mathematical addition. Hydration and gender interaction on CRT errors. Mild and varied effects of hydration status with slight decrements in vigilance attention and slight enhancements in STM.
D'Anci, et al., (Study 2) (2009)	12 M & 12 F	60min high intensity rowing or 75min of lacrosse drills	1.2% BW	STM, CRT, Spatial Memory, Vigilance Attention, Visual Perception	After Exercise	Abstinence from alcohol for 24hrs, caffeine for 6hrs and tobacco for 2hrs prior to testing. 1L of water received on test day to be consumed prior to testing. Following dehydration, half of participants received a candy (25g glucose).	Yes	No effects of hydration condition, gender, or glucose on digit span, mental rotation or CRT performance. Fewer errors on some tasks with glucose (map memory for females, continuous performance task for both genders). No consistent effects of glucose on cognition.

Table 2.2b. *(continued)*

Study	Subjects (*n*)	Dehydration Intervention	Dehydration Level	Cognitive Task	Time of Test	Conditions	Impairment with Dehydration	Findings
Ganio, et al., (2011)	26M	3 x 40min treadmill walks at 5.6km/hr, 5% grade, 28°C	1.59% BW	Scanning visual vigilance, Psychomotor vigilance, 4 Choice visual RT, MTS, Repeated Acquisition, Grammatical Reasoning	During & 20min After Exercise	Refrained from caffeine and alcohol for 12hrs before each session. No exercise during the 24hrs before each experiment. Consumed standard meals, with fluid type and volume specified, for 24hrs before each test session. Consumed 240ml supplemental water on each night before testing and 240ml of water upon waking on the morning of testing.	Yes	Dehydration degraded visual working memory response latency and errors increased in visual vigilance. Fatigue increased in men (POMS).
Kempton, et al., (2011)	5 M & 5 F	90min Exercise – cycling at 130W for 50min, 10min recovery, 20min cycling at 130W, 10min recovery	0.53% BW = C, 1.64% BW = Ex	Tower of London task - RT	Before and After Exercise	Maintained normal diet, avoid alcohol and strenuous physical activity for 24hrs prior. Instructed to consume 500ml water the evening prior and 500ml water 1hr prior to testing. BOLD fMRI and sMRI tests completed during cognitive tests.	No	Reaction time improved after exercise, no effects on percentage of errors or number of trials achieved.
Armstrong, et al., (2012)	25 F	3 x 40min treadmill walks at 5.6km/hr, 5% grade, 28°C	1.39% BW	Scanning visual vigilance, Psychomotor vigilance, 4 Choice visual RT, MTS, Repeated Acquisition, Grammatical Reasoning	Before, During & 20min After Exercise	Refrained from caffeine and alcohol for 12hrs before each session. Consumed same meal for 24hrs before each test session. Consumed 240ml supplemental water on each night before testing and 240ml of water upon waking on the morning of testing. Standardised bkfast provided morning of testing.	No	Dehydration resulted in sig. differences in POMS scores (mood, tension, vigour, fatigue, confusion) and VAS (task difficulty, concentration, headache) compared to control. No differences were observed in cognitive performance on the CTB between trials.

Exercise + Heat Stress Induced Dehydration

Study	Subjects (*n*)	Dehydration Intervention	Dehydration Level	Cognitive Task	Time of Test	Conditions	Impairment with Dehydration	Findings
Leibowitz, et al., (1972)	4 M & 4 F	20min walking periods over 6hrs of treadmill exercise in a heat chamber	2.7, 4.2% BW	CRT	During the first and last 5min of every other 20min walking period and during 2hrs post exercise	2 subjects obese and 2 lean from each gender.	No	No sig effect of dehydration on RT. Faster response time to peripheral visual stimuli, no effect on response time to central visual stimuli.
Sharma, et al., (1986)	8 M	15 steps/min on 38cm high stool in climatic chamber (45°C, 30% RH = HD or 39°C, 60% RH = HH)	1.3, 1.4, 2.2, 2.3, 3.3% BW	Substitution test, Concentration test, Psychomotor test	90min post exercise	8 days of heat acclimatisation - performing moderate work. After dehydration, rested in thermoneutral room for 90min. Completed test battery in thermoneutral room after dehydration.	Yes	Sig and progressive decrease in concentration and coordination at 2-3% dehydration.
Gopinathan, et al., (1988)	11 M	15 steps/min on 38cm high stool in climatic chamber (45°C, 30% RH)	1.3, 2.4, 3.3, 4.3 % BW	Word recognition test, Serial addition test, Trail-making test	Before & After Exercise	8 days of heat acclimatisation - performing step up/down for 2hrs/day (2 x 50min work with 10min rest between). After dehydration, rested in thermoneutral room until recovered (return to HRrest and resting oral temp). Completed test battery in thermoneutral room before and after dehydration.	Yes	STM progressively deteriorated as degree of dehydration increased with 2% reported as critical level for sig. results. Serial addition test results followed same pattern, with sig. fall in efficiency at 2% and again at 4% dehydration. Trail making test speed decreased as dehydration level increased with sig. first seen at 2%.
Solera, et al., (1999)	23 M	90min cycling exercise at 70% HRmax (28°C, 100% RH)	1.78% BW	Reaction time, Visual perception, and Auditive memory	Before, During (every 30min) and After Exercise	-	Yes	Reaction time improved as the exercise period progressed but was significantly faster when the persons were hydrated. Results were not significant for the other cognitive tests.

Table 2.2b. *(continued)*

Study	Subjects (*n*)	Dehydration Intervention	Dehydration Level	Cognitive Task	Time of Test	Conditions	Impairment with Dehydration	Findings
Zuri, et al., (2004)	10 M	45 – 120min treadmill exercise with limited fluid intake in a hot, humid environment	3.27% BW	Headminder CSI – RT, processing speed, memory, attention/executive functioning	Before and Following Recovery (rest in air con room until heat and exercise effects subsided)	Abstained from alcohol, caffeine, non-prescription medication and dehydrating behaviours for 24hrs pre and duration of study.	Yes	Improvements and decrements in cognitive performance observed with dehydration. Processing speed improved, symbol scanning response time improved, response direction 1 revealed impairment.
McMorris, et al., (2006)	8 M	2hrs heat exposure (36°C, 75% RH) with 2x 20min bouts of cycling at 100W	2.75% BW	RMG test – working memory, central executive performance, Verbal and spatial STM, CRT	Before, 15min After dehydration intervention and After rehydration	Refrained from alcohol for 24hrs and caffeine products on the morning of the test. Instructed to drink 500ml non-alcoholic liquid the night before. Eat and drink as normal for breakfast. Habituation completed 48hrs prior.	Yes	Deteriorated performance following heat stress dehydration on central executive task, but not on verbal and spatial recall and CRT tasks.
Serwah, et al., (2006)	8 M	Cycling at 70% PPO for 90min or until exhaustion in heat chamber (31°C, 63% RH)	0.2% BW = 100% FR, 1.0% BW = 50% FR, 1.7% BW = 0% FR	CRT	Before, During (every 20min) and After Exercise	Drank tap water ad lib. night before until 1hr prior to trial.	No	No difference in CRT between any of the conditions. CRT facilitated as duration of exercise increased. CRT and accuracy negatively affected by number of choices.
Baker, et al., (2007)	11 M	9 x 15min bouts of walking at 50% VO2max in the heat (40°C, 20% RH) with 5min rest intervals + 80min of basketball game simulated drills	1, 2, 3, 4% BW	VIP, Attention, RT	Before, After walking exercise and After basketball drills exercise	Std bkfast + 5ml/kg water prior to pre test and exercise.	Yes	In the target-infrequent half of the post basketball test, dehydration resulted in sig deficits in sensitivity, slower RT, and more omission errors compared to euhydrated trials. In the target-frequent half of test 3 dehydration resulted in slower RT and less sensitivity than euhydration trials, and in test 2 more omission errors and commission errors were made in dehydrated conditions.
Tomporowski, et al., (2007)	11 M	15, 60 or 120min cycling at 60% VO2max followed by GXT to exhaustion in environmental chamber (30°C, 40%RH)	15min NF = 1.27% BW, 60min NF = 2.27% BW, 120min NF = 3.67% BW, 120min FC = 0.69% BW	Executive Processing - Category Switching Test, STM	Before & within 5min After Exercise/Fluid Ingestion	Fasted 3hrs prior to testing. 7% CHO solution (volume pre-determined by sweat rate at familiarisation) consumed in F trial.	No	No differences in switch cost cognitive performance based on hydration condition however, switch cost decreased sig. following exercise. Frequency of choice response errors increased sig. following exercise regardless of hydration condition. Errors increased more during switch trials compared to non switch trials. Item recall improved following exercise but decreased as a function of delay interval. No differences based on hydration condition.
Adam, et al., (2008)	6 M & 2 F	3hrs passive heat exposure without fluid (45°C, 50% RH) + 60min cycle exercise (TEE = 550kcal)	3% BW	Target detection latency, accuracy of shots, total response latency, friend-foe discrimination, no. of targets detected, Scanning visual vigilance	After 5min in environment (hot or cold)	Std bkfast + water ad lib provided 1hr prior to testing. Following heat exposure a 2hr recovery period was given where a shower was permitted and a small snack + 200ml water given.	No	Moderate dehydration had no effect on cognitive and psychomotor performance in either hot or cold environments.

Table 2.2b. *(continued)*

Study	Subjects (*n*)	Dehydration Intervention	Dehydration Level	Cognitive Task	Time of Test	Conditions	Impairment with Dehydration	Findings
Bandelow, et al., (2010)	20 M	Football game (34°C, 64% RH)	Up to 2.5% BW	Visual sensitivity, Fine motor speed, Visual/auditory working memory, Visuo-spatial working memory	Before, During (at half time) and After football match	Three hours before each game, participants ate a small, standardised meal and drank only water. To ensure good hydration status, they were encouraged to drink water liberally the night before the game. During the match period, all players could consume water ad lib.	Yes	Finger-tapping speed increased with dehydration. On the Sternberg test, simple RT with the lowest WM load increased with increasing dehydration level and the opposite effect was found for high WM loads.
Caldwell, et al., (2011)	9 M	1.5hrs treadmill walking at 2 km/hr + 1hr treadmill walking at 4 km/hr in a hot environment (36°C, 60% RH) and wearing military style clothing	1.65-2.19% BW	Mini-Cog rapid assessment battery – vigilance, three term reasoning, filtering, verbal working memory, divided attention, perceptual reaction time	Before & at 30min intervals throughout exercise	Refrained from strenuous exercise, alcohol consumption, and tobacco 12hrs before each trial. On the night before a trial, subjects consumed 15ml/kg of additional water and ate an evening meal and breakfast high in carbohydrate and low in fat. Refrained from caffeine for 2hrs before testing. Subjects were provided with 500ml of water on arrival to lab and consumed 500ml of water after each 30min of exercise.	No	No effect of dehydration on any measures of cognitive performance.
Jimenez-Pavon, et al., (2011)	16 M	40 – 60 min treadmill running at 60% MAS in a hot environment (35°C, 60% RH)	2.4% BW	Vienna test system - SRT, CRT, Multiple reaction time and rate of correct/incorrect reactions, Peripheral vision reaction time, Field of vision, left and right visual angle	Before & 15min After exercise	Avoid strenuous exercise, Refrain from alcohol & medication in the 2 days prior to the study. Follow a hydration protocol with body mass assessed over a period of 1 week to ensure hydrated state.	Yes	After the running bout, complex and peripheral reaction time consistently improved, but visual angle was impaired.
MacLeod, et al., (2012)	8 F	121±10 min passive hyperthermia (40°C, 75% RH) and controlled fluid intake 1 day preceding testing + 50 min field hockey-specific intermittent treadmill running in hot environmental conditions (33°C, 60% RH)	2% BW	Field hockey skill performance test (decision making time)	During Exercise	Recorded food and drink consumption for 2 days before initial trial and repeated before the remaining trial. Abstained from intense exercise, alcohol and caffeine for 48hrs before each trial and were instructed to drink at least 2 L of water per day for 3 days prior to trials.	Yes	Decision making time was significantly increased in dehydration trial compared to euhydrated conditions.
Morley, et al. (2012)	10 M	Treadmill walk in a heated room (33 - 35°C) for up to 50 min at a speed of 4.5 km/hr wearing thermal protective clothing	1.6% BW	Paced auditory serial addition test (sustained & divided attention), repeated episodic memory test (STM, new learning, recognition memory, susceptibility to interference), Walter Reed psychomotor vigilance test (reaction time)	Immediately Before & After Exercise	Refrained from caffeine, alcohol, and nicotine for 12hrs prior to trials.	No	No effect of dehydration on any measures of cognitive performance.
Morley, et al. (2012)	14 M, 5 F	Treadmill walk in a heated room (33 - 35°C) for 20min at 4.5 km/hr, 6 min at 2.5 km/hr, and then until 50 min total exercise at 4.5 km/hr wearing thermal protective clothing	0.6% BW	Paced auditory serial addition test (sustained & divided attention), repeated episodic memory test (STM, new learning, recognition memory, susceptibility to interference), Walter Reed psychomotor vigilance test (reaction time)	Before, Immediately After, and serially up to 120 min After Exercise (30, 60, 90, 120 min).	Refrain from caffeine, alcohol, and nicotine for 12hrs prior to trials. After exercise, water provided equal to the volume lost during exercise and consumed in equal portions every 5min for 20min total.	Yes	Mean of the 10 slowest reaction times progressively lengthened during recovery. Sustained & divided attention modestly improved immediately and 30 min after exercise. No changes in short-term memory identified immediately after exercise but fewer correct words recalled 60 and 120 min after exercise.

Table 2.2b. *(continued)*

Study	Subjects (*n*)	Dehydration Intervention	Dehydration Level	Cognitive Task	Time of Test	Conditions	Impairment with Dehydration	Findings
Fluid Deprivation + Exercise Induced Dehydration								
Banderet, et al., (1984)	18 M	Severe fluid restriction and exercise induced sweating over 10hrs	2.5% BW	Coding, Number comparison, Grammatical reasoning, Computer interaction, and Pattern comparison tasks	Over 5 days, 2-3min after 15min of exercise interspersed throughout	Subjects given adequate food but were limited in the fluid intake permitted.	Yes	Dehydration or cold exposure with limited fluid intake impairs cognitive performance. Dehydration before cold exposure resulted in a sig 10-21% decrement in performance for all tests except grammatical reasoning. Dehydration and cold exposure resulted in 19-29% decrements in performance which was comparable to just cold exposure alone.
Patel, et al., (2007)	24 M	Fluid restriction for 15hrs + 45min cycling at 65-70% HRmax	2.5% BW	GSC, SAC, ANAM, BESS, SOT	25min post exercise	15hrs fasted, abstinence from alcohol and caffeine, std. bkfast provided 20min prior to exercise.	Yes	No differences in SAC, BESS, SOT and composite ANAM scores between conditions. Subjects in dehydrated state had sig. deterioration in visual memory and fatigue measures assessed in the ANAM. Higher no. and greater symptoms for dehydration on the GSC.
Exercise + Diuretic Induced Dehydration								
Ganio, et al., (2011)	26M	3 x 40min treadmill walks at 5.6km/hr, 5% grade, 28°C with 40mg furosemide	1.59% BW	Scanning visual vigilance, Psychomotor vigilance, 4 Choice visual RT, MTS, Repeated Acquisition, Grammatical Reasoning	Before, During & 20min After Exercise	Refrained from caffeine and alcohol for 12hrs before each session. No exercise during the 24hrs before each experiment. Consumed standard meals, with fluid type and volume specified, for 24hrs before each test session. Consumed 240ml supplemental water on each night before testing and 240ml of water upon waking on the morning of testing.	Yes	Dehydration degraded visual working memory response latency and errors increased on visual vigilance. Fatigue increased in men (POMS).
Armstrong, et al., (2012)	25 F	3 x 40min treadmill walks at 5.6km/hr, 5% grade, 28°C with 40mg furosemide	1.39% BW	Scanning visual vigilance, Psychomotor vigilance, 4 Choice visual RT, MTS, Repeated Acquisition, Grammatical Reasoning	Before, During & 20min After Exercise	Refrained from caffeine and alcohol for 12hrs before each session. Consumed same meal for 24hrs before each test session. Consumed 240ml supplemental water on each night before testing and 240ml of water upon waking on the morning of testing. Std. bkfast provided morning of testing.	No	Dehydration resulted in sig. differences in POMS scores (mood, tension, vigour, fatigue, confusion) and VAS (task difficulty, concentration, headache) compared to control. No differences were observed in cognitive performance on the CTB between trials.

Table 2.4 Abbreviations:

Ad lib. = ad libitum	CTB = cognitive test battery	HRrest = resting heart rate	PPO = peak power output	STM = short term memory
BESS = balance error scoring system	F = female	LTM = long term memory	RH = relative humidity	Tcore = core body temperature
Bkfast = breakfast	FC = fluid provided condition	M = male	RMG = random movement generation	TEE = total energy expenditure
BOLD = blood oxygen level dependent	fMRI = functional magnetic resonance imaging	MAS = maximal aerobic speed	RT = reaction time	VAS = visual analogue scale
BW = body weight	FR = fluid replacement	MR = mouth rinse condition	SAC = standardised assessment of concussion	VIP = visual information processing
C = control condition	GSC = graded symptom checklist	MT = morning tea	Sig. = significant	VT = ventilatory threshold
CFF = critical flicker fusion	GXT = graded exercise test	MTS = match to sample	sMRI = structural magnetic resonance imaging	W = watts
CHO = carbohydrate	HD = hot dry	NaCl = sodium chloride	SOT = sensory organisation test	WM = working memory
CRT = choice reaction time	HH = hot humid	NF = no fluid provided condition	SRT = simple reaction time	YYIRT = YoYo intermittent recovery test
CSI = cognitive stability index	HR_{max} = maximum heart rate	POMS = profile of mood states	Std. = standardised	

Given the available evidence, there is some difficulty in summarising the information and drawing conclusions about the effects of dehydration on cognitive performance. Individual research studies have employed vastly different study designs that may be partly responsible for the conflicting results that have been observed (e.g. level and method of dehydration, the timing and tasks involved in cognitive testing, differences in participant characteristics such as age, gender, intelligence). A small number of review papers summarising the dehydration and cognitive performance literature also highlight this fact (Maughan, 2003; Tomporowski, 2003; Wilson & Morley, 2003; Sawka, 2004; Ritz & Berrut, 2005; Grandjean & Grandjean, 2007; Lieberman, 2007; Maughan, Shirreffs, & Watson, 2007; Murray, 2007; Sawka et al., 2007; Shirreffs, 2009).

2.2.4.1 Level of Dehydration

The level of dehydration that occurs with physical exertion depends greatly on the amount of sweat lost and rate of any fluid ingestion (Lieberman, 2007). One of the most apparent observations from the body of literature investigating dehydration and cognitive performance is the large variation in dehydration level evoked within studies. The use of dose-response protocols to assess threshold levels for which specific cognitive deficit occurs has contributed to this range reported. As various levels of dehydration may differentially affect individual cognitive processes (Lieberman, 2007), it is difficult to compare the results of individual studies where dehydration levels are clearly different.

All 29 studies investigating the effects of exercise-induced dehydration on cognitive performance report dehydration levels based on changes in body weight. The mean dehydration level reported across the 29 studies ranged between 0.2% and 4.3% loss in body weight incorporating a total of 67 individual trials. Of these, no impairment was found in 39 (58%) trials and a significant impairment in performance on one or more cognitive tasks was observed in 28 (42%) trials. Tables 2.2c and 2.2d show the individual trials from the 29 studies, corresponding

dehydration levels, dehydration interventions used, and the cognitive tasks where no impairment

and significant impairment in cognitive performance was observed respectively.

Table 2.2c. Summary of research studies reporting no impairment in cognitive performance following dehydration

Study	Dehydration Level *	Dehydration Intervention	Cognitive Tasks	Cognitive Domains
Serwah, et al., (2006)	0.2% BW	Exercise + Heat	Choice reaction time	Reaction
Adam, et al., (2008)	0.3% BW	Exercise + Heat	Target shooting speed and accuracy, Scanning visual vigilance	Target Shooting, Attention
Kempton, et al., (2010)	0.53% BW	Exercise	Executive function (Tower of London), Reaction time	Executive Function, Reaction
Morley, et al., (2012)	0.6% BW	Exercise + Heat	Sustained attention, divided attention, short term memory, new learning, recognition memory, susceptibility to interference, psychomotor vigilance	Attention, Memory, Reaction
Tomporowski, et al., (2007)	0.69% BW	Exercise + Heat	Short term memory	Memory
Edwards, et al., (2007)	0.73% BW	Exercise	Mental concentration	Attention
Serwah, et al., (2006)	1% BW	Exercise + Heat	Choice reaction time	Reaction
D'Anci, et al., (2009)	1.2% BW	Exercise	Short term memory, Spatial memory, Vigilance, Divided attention	Memory, Attention
Tomporowski, et al., (2007)	1.27% BW	Exercise + Heat	Short term memory	Memory
Sharma, et al., (1986)	1.3% BW	Exercise + Heat	Concentration, Eye-hand coordination, Symbol classification efficiency	Memory, Perception, Motor skills
Gopinathan, et al., (1988)	1.3% BW	Exercise + Heat	Short term memory, Arithmetic efficiency, Trail Making	Memory, Math, Executive Function
Armstrong, et al., (2010)	1.39% BW	Exercise & Exercise + Diuretics	Scanning visual vigilance, psychomotor vigilance, Choice reaction time, Match to sample, Repeated acquisition, Grammatical Reasoning	Attention, Reaction, Memory, Other
Sharma, et al., (1986)	1.4% BW	Exercise + Heat	Concentration, Eye-hand coordination, Symbol classification efficiency	Memory, Perception, Motor skills
Morley, et al., (2012)	1.6% BW	Exercise + Heat	Sustained attention, divided attention, short term memory, new learning, recognition memory, susceptibility to interference, psychomotor vigilance	Attention, Memory, Reaction
Kempton, et al., (2010)	1.64% BW	Exercise	Executive function (Tower of London), Reaction time	Executive Function, Reaction
Serwah, et al., (2006)	1.7% BW	Exercise + Heat	Choice reaction time	Reaction
Caldwell, et al., (2011)	1.65% BW	Exercise + Heat	Vigilance, three term reasoning, filtering, verbal working memory, divided attention, perceptual reaction time	Memory, Reaction, Attention, Other
Solera, et al., (1999)	1.78% BW	Exercise + Heat	Auditive memory, Visual Perception	Memory, Perception
D'Anci, et al., (2009)	1.8% BW	Exercise	Short term memory, Simple reaction time, Choice reaction time, Map planning, Mathematical addition, Visual perception	Memory, Reaction, Executive Function, Math, Perception

Table 2.2c. *(continued)*

Study	Dehydration Level *	Dehydration Intervention	Cognitive Tasks	Cognitive Domains
Edwards, et al., (2007)	2.14% BW	Exercise	Mental concentration	Attention
Sharma, et al., (1986)	2.2% BW	Exercise + Heat	Symbol classification efficiency	Perception
Grego, et al., (2005)	2.2% BW	Exercise	Map recognition speed	Reaction
Tomporowski, et al., (2007)	2.27% BW	Exercise + Heat	Short term memory	Memory
Sharma, et al., (1986)	2.3% BW	Exercise + Heat	Symbol classification efficiency	Perception
Edwards, et al., (2007)	2.4% BW	Exercise	Mental concentration	Attention
Jiménez-Pavón, et al., (2011)	2.4% BW	Exercise + Heat	Simple reaction time, Choice reaction time, Multiple reaction time, Peripheral vision reaction time	Reaction
Banderet, et al., (1984)	2.5% BW	Fluid deprivation + Exercise	Grammatical Reasoning	Other
Patel, et al., (2007)	2.5% BW	Fluid deprivation + Exercise	Simple reaction time, Math processing, Sternberg memory, Orientation, Immediate memory, Concentration, Delayed recall	Reaction, Math, Memory, Perception, Attention
Bandelow, et al., (2010)	2.5% BW	Exercise + Heat	Visual sensitivity, Fine motor speed, Visual/auditory working memory, Visuo-spatial working memory	Reaction, Memory, Perception, Attention
Leibowitz, et al., (1972)	2.7% BW	Exercise + Heat	Central & peripheral reaction time	Reaction
McMorris, et al., (2006)	2.75% BW	Exercise + Heat	Verbal & Spatial recall, Choice reaction time	Memory, Reaction
Cian, et al., (2000)	2.8% BW	Exercise	Choice Reaction time	Reaction
Cian, et al., (2001)	2.8% BW	Exercise	Long term memory, Choice reaction time, Unstable tracking	Memory, Reaction, Motor Skills
Adam, et al., (2008)	3.0% BW	Exercise + Heat	Target shooting speed and accuracy, Scanning visual vigilance	Target Shooting, Attention
Zuri, et al., (2004)	3.27% BW	Exercise + Heat	Processing speed	Reaction
Sharma, et al., (1986)	3.3% BW	Exercise + Heat	Symbol classification efficiency	Perception
Tomporowski, et al., (2007)	3.67% BW	Exercise + Heat	Short term memory	Memory
Grego, et al., (2005)	4.1% BW	Exercise	Map recognition speed	Reaction
Leibowitz, et al., (1972)	4.2% BW	Exercise + Heat	Central & peripheral reaction time	Reaction

* Measured as mean % loss in body weight from baseline measures. BW = Body Weight. Fluid deprivation refers to an isolated period of extended fluid intake restriction.

Table 2.2d. Summary of research studies reporting significant impairment in cognitive performance following dehydration

Study	Dehydration Level *	Dehydration Intervention	Cognitive Task	Cognitive Domains
Tomporowski, et al., (2007)	0.69% BW	Exercise + Heat	Executive processing choice response	Reaction
Baker, et al., (2007)	1% BW	Exercise + Heat	Vigilance related attention, Response time	Attention, Reaction
Tomporowski, et al., (2007)	1.27% BW	Exercise + Heat	Executive processing choice response	Reaction
Ganio, et al., (2011)	1.59% BW	Exercise & Exercise + Diuretics	Visual working memory response latency, Visual vigilance errors	Memory, Attention
Solera, et al., (1999)	1.78% BW	Exercise + Heat	Reaction time	Reaction
D'Anci, et al., (2009)	1.8% BW	Exercise	Vigilance	Attention
Baker, et al., (2007)	2% BW	Exercise + Heat	Vigilance related attention, Response time	Attention, Reaction
MaacLeod, et al., (2012)	2% BW	Exercise + Heat	Decision making time	Reaction
Sharma, et al., (1986)	2.2% BW	Exercise + Heat	Concentration, Eye-hand coordination	Memory, Perception
Grego, et al., (2005)	2.2% BW	Exercise	Perceptual response, Map recognition response errors	Perception, Other
Tomporowski, et al., (2007)	2.27% BW	Exercise + Heat	Executive processing choice response	Reaction
Sharma, et al., (1986)	2.3% BW	Exercise + Heat	Concentration, Eye-hand coordination	Memory, Perception
Gopinathan, et al., (1988)	2.4% BW	Exercise + Heat	Short term memory, Arithmetic efficiency, Trail Making	Memory, Math, Executive Function
Jiménez-Pavón, et al., (2011)	2.4% BW	Exercise + Heat	Visual angle	Perception
Banderet, et al., (1984)	2.5% BW	Fluid deprivation + Exercise	Coding, Number comparison, Computer interaction, Pattern comparison	Other
Patel, et al., (2007)	2.5% BW	Fluid deprivation + Exercise	Match to sample , Sleep scale	Memory, Other
Bandelow, et al., (2010)	2.5% BW	Exercise + Heat	Visual/auditory working memory test speed	Reaction
McMorris, et al., (2006)	2.75% BW	Exercise + Heat	Working memory (Random movement generation test)	Memory
Cian, et al., (2000)	2.8% BW	Exercise	Short term memory, Long term memory, Perceived discrimination, Unstable tracking	Memory, Perception, Motor Skills
Cian, et al., (2001)	2.8% BW	Exercise	Short term memory, Perceived discrimination	Memory, Perception
Baker, et al., (2007)	3% BW	Exercise + Heat	Vigilance related attention, Response time	Attention, Reaction

Table 2.2d. *(continued)*

Study	Dehydration Level *	Dehydration Intervention	Cognitive Task	Cognitive Domains
Zuri, et al., (2004)	3.27% BW	Exercise + Heat	Response speed	Reaction
Sharma, et al., (1986)	3.3% BW	Exercise + Heat	Concentration, Eye-hand coordination	Memory, Perception
Gopinathan, et al., (1988)	3.3% BW	Exercise + Heat	Short term memory, Arithmetic efficiency, Trail Making	Memory, Math, Executive Function
Tomporowski, et al., (2007)	3.67% BW	Exercise + Heat	Executive processing choice response	Reaction
Baker, et al., (2007)	4% BW	Exercise + Heat	Vigilance related attention, Response time	Attention, Reaction
Grego, et al., (2005)	4.1% BW	Exercise	Perceptual response, Map recognition response errors	Perception, Other
Gopinathan, et al., (1988)	4.3% BW	Exercise + Heat	Short term memory, Arithmetic efficiency, Trail Making	Memory, Math, Executive Function

* Measured as mean % loss in body weight from baseline measures. BW = Body Weight. Fluid deprivation refers to an isolated period of extended fluid intake restriction.

Of the literature reporting impairment in cognitive performance following exercise-induced dehydration (Table 2.2d), it appears that adverse effects are present with dehydration levels as low as 0.69% BW loss. Several studies have also reported no observations in cognitive impairment across many dehydration levels. This evidence is particularly prevalent for dehydration levels less than 2% BW loss, with 15 (68%) studies reporting no cognitive impairment compared to 5 (29%) studies that did observe decrements in performance. With dehydration greater than 2% BW loss, there is more consistency between studies, with 22 (33%) trials showing cognitive performance decrements following dehydration. Based on these findings, studies investigating the effects of dehydration on cognitive performance should ensure that appropriate methods are employed to induce levels of dehydration above 2% BW loss. This will provide the best opportunity to determine the effects of dehydration on cognitive performance.

2.2.4.2 Method of Dehydration

Most studies examining the effects of dehydration on cognitive performance have employed dehydration methods involving an acute bout of exercise to facilitate sweat loss. The effects of the resulting dehydration provide some evidence for impairment on a range of cognitive performance tasks. However, the impact of physical activity itself on cognitive performance is complex. As such controversy exists regarding the overall cognitive outcomes associated with exercise, with evidence supporting a positive effect of acute exercise on cognitive function (Etnier et al., 1997; Lambourne & Tomporowski, 2010; Chang et al., 2012). The inconsistencies reported result from a multitude of factors associated with the physical activity (intensity, duration, type of exercise), type and timing of cognitive tests, and differences in subjects (background and fitness level) used across studies. It is therefore important to account for all perturbations that result from an exercise task when investigating changes in cognitive performance that may result from dehydration.

Methodological Differences in Studies Employing an Exercise-Induced Dehydration Protocol

While most studies have employed an exercise task within their method, only some (31%) have done this in isolation. A greater proportion (69%) of studies examining dehydration and cognitive performance have used a combination of stressors to induce dehydration (e.g. exercise + heat, exercise + diuretics, exercise + extended fluid deprivation). The majority of these (55%) have been a combination of exercise and heat stress. This is often done in a climatic chamber incorporating a heat component to hasten the rate of sweat loss and therefore dehydration. However, a combination of these stressors may have complex, non-linear effects on cognitive performance (Lieberman, 2007). For example, when dehydration is induced by exercise in a hot environment, the heat stress component itself may provide additional cognitive burden that influences overall study results. Thus, cognitive performance changes observed when testing is conducted during or immediately after exercise with heat exposure may not be entirely associated with dehydration.

In addition, studies employing exercise methods to promote fluid loss may have uncontrollable stressors related to the act of physical exertion itself, such as thermal effects or fatigue. Dehydration increases core body temperature responses during exercise in temperate and climatic environments (Sawka & Coyle, 1999). As it is impossible to prevent these stressors during physical activity, studies examining cognitive performance after exercise that do not allow adequate recovery or cooling to offset thermal and fatigue components cannot be interpreted as studies of dehydration per se. It follows then that very few studies have strictly investigated the effects of exercise-induced dehydration in isolation and its impact on cognitive functioning. Grandjean & Grandjean (2007) acknowledged this in a recent review on dehydration and cognitive performance by stating "A major limitation of most studies conducted to date is the inability to determine the effects of dehydration independent of the effects of thermal stress, physical stress, and/or fatigue" (p. 552).

2.2.4.3 Dehydration and Discrete Cognitive Tasks

A number of studies (*n*=9) have attempted to investigate the effects of dehydration on cognitive performance independent of other stressors. These studies normally employ an exercise component in a thermo-neutral environment with monitoring of body temperatures to ensure physiological strain is not influenced by a heat stress. In addition, a period of recovery following physical exertion is included prior to the application of cognitive performance tests. Of these studies, only five found that exercise induced dehydration independently resulted in cognitive performance impairment (Cian et al., 2000; Cian et al., 2001; Grego et al., 2005; D'Anci et al., 2009; Ganio et al., 2011).

Two exemplar studies are those of Cian et al., (2000; 2001). In the first of these studies, eight male participants were dehydrated (2.8% BW loss) by treadmill exercise at 60% VO_{2max} for ~2hrs in a thermo-neutral environment (25-26°C, 35-45% relative humidity (RH)). Following exercise, participants were given 30 min recovery before cognitive test batteries involving Choice Reaction Time (CRT), Short-Term Memory (STM), Long-Term Memory (LTM), perceptive discrimination, and unstable tracking were administered. Core body temperature was monitored throughout exercise and recovery, and cognitive tests were performed with core temperatures of 37.13 ± 0.4°C (dehydration trial) and 36.9 ± 0.24°C (control trial; no exercise and fluid replacement to recover body weight losses over the 2hr resting period). Compared to control trials, dehydration resulted in impaired cognitive abilities (unstable tracking, perceptive discrimination, STM). A trend was also observed for impairment in CRT, however the main effect of hydration status was not reliable and the task used was considered to be an insensitive measure. There were no differences in LTM measures of free recall and recognition between trials. Subjective ratings of fatigue were significantly higher in the dehydration trial compared to control, whilst no differences were observed in mood status between the two trial conditions. The results of this study suggest that

exercise induced dehydration resulting in a body water deficit of 2.8% BW loss causes a reduction in performance level for various fundamental cognitive abilities.

A year later, Cian et al., (2001) used a similar study design to examine the effects of different dehydration and fluid replacement protocols on cognitive function in seven male participants. Cognitive testing was completed following dehydration with core body temperatures below 38°C. After the initial cognitive testing phase, participants were either provided with a beverage intended to cause complete rehydration of fluid losses or were kept in a dehydrated state (2.42 ± 0.27% BW loss). A control condition was also included, which involved no exercise and fluid replacement to recover body weight losses over the time period. Consistent with their previous findings, the results from this study suggest that exercise induced dehydration of 2.8% BW loss has detrimental effects on cognitive performance (perceptive discrimination, STM) compared to control conditions. However, it is also noted that some of these impairments disappear with time (i.e. STM). In addition, when fluid replacement is administered following dehydration there appears to be no beneficial effect on cognitive performance measures of perception discrimination (decision reaction time), however an improvement in LTM is observed.

One of the major limitations in the abovementioned studies is the small number of participants included (n=8 and n=7). Given there is often a high degree of individual variability in response to cognitive tasks, the number of participants may not have been sufficient to observe impairment in some of the individual tests, thus inducing a type II statistical error. This may explain why no significant results were observed between trials for tasks such as the CRT test. Another limitation of these studies is that it is not possible to determine the effect of dehydration independent of fatigue. The initial cognitive tests were completed 30 min after exercise, which may not have allowed enough recovery from the stress of the exercise itself, especially in participants unaccustomed to endurance exercise. In the more recent of the studies, subjective ratings of fatigue were reduced when fluid was ingested post exercise. However, whilst 100% of the fluid

loss was replaced in these trials, participants were not completely rehydrated, with a 0.52 ± 0.38% BW loss still present during the second cognitive test battery. A rehydration protocol providing time to allow complete recovery of water losses may lead to different findings.

To examine the influence of exercise induced dehydration on cognitive function, Grego et al., (2005) compared results from protocols involving fluid replacement (2200ml mineral water) and no fluid intake conditions during exercise in a group of 8 male endurance trained participants. A 3hr exercise cycle at 60% VO_{2max} in a temperature controlled environment (~20-21°C, 50 ± 5% RH) was used to induce 4.1% and 2.2% BW loss dehydration for the no fluid and fluid trials respectively. Cognitive performance using perceptual response and map recognition tasks were completed before, throughout and within 5 min of completion of the exercise. Rectal temperatures were recorded pre and post exercise and cognitive tests were completed at these times with core body temperatures of 37.1 ± 0.1°C and 37.3 ± 0.2°C for the pre exercise fluid and no fluid conditions respectively and 37.6 ± 0.3°C and 37.9 ± 0.3°C for the post exercise fluid and no fluid conditions respectively. The differences in core body temperature pre and post exercise for both trial conditions were significant. No differences in cognitive performance were reported between the two trial conditions (fluid and no fluid) pre and post exercise and the results were therefore combined to give an overall effect of dehydration. Compared to pre trial cognitive tests, dehydration caused significant impairment in perceptual response. Map recognition ability was also impaired by dehydration with an increase in the number of errors made on the task. However, response time on the map recognition task improved with dehydration, which indicated a trade off between speed and accuracy. No subjective measures of fatigue were recorded in this study. However, cognitive tests were administered within 5 min post exercise and significant differences were reported between pre and post core body temperatures. This may indicate an influence of exercise related heat stress on cognitive performance.

A recent study by Ganio et al., (2011) found that dehydration of 1.59% BW loss induced by exercise was sufficient to cause subtle adverse effects on visual working memory, visual vigilance and perception of fatigue. Twenty-six male participants completed three 40min treadmill walks in a temperature controlled room at 28°C until a weight loss of >1% BW occurred. Twenty minutes after the completion of exercise, the participants' cognitive functions were assessed as well as subjective measures of fatigue, mood and body symptoms (headache, concentration, task difficulty). Results from the study indicated a significant difference compared to control conditions (exercise and body weight maintained with water ingestion). A slowing of visual working memory response latency and an increase in visual vigilance errors was observed in dehydration trials compared to control conditions. In addition, subjective ratings of fatigue were significantly higher with dehydration compared to the control trials. Dehydration had no effect on cognitive function for behavioural tasks involving CRT, learning and logical reasoning. Again, the effect of dehydration on cognitive performance in this study may have been influenced by exercise induced fatigue and may not be a reflection of dehydration. While cognitive testing was performed in a thermo-neutral environment (23°C), administration of the cognitive test battery occurred 20 min post physical exertion and may not have allowed adequate recovery from the exercise protocol. Thus, the effects of dehydration on cognitive performance variables in this study may have been influenced by other factors.

2.2.4.4 Dehydration and Driving Performance

Given the evidence for dehydration induced decrements in some discrete cognitive skills, it is possible that the effects of dehydration translate to broader and more applied cognitive tasks (i.e. driving a motor vehicle). However, despite awareness for the likelihood of dehydration in the order of 5-10% BW loss during motor racing events (Klarica, 2001; Rodrigues & Magalhães, 2004; Allen & White, 2010), the direct impact of dehydration on driving performance is yet to be

investigated. Several studies have examined driving performance during extended periods in hot environmental conditions (Mackie & O'Hanlon, 1977; Wyon et al., 1996; Walker et al., 2001; Daanen et al., 2003). As a collective, these studies indicate systematically poorer driving performance when individuals experience a concurrent heat stress. Greater steering adjustments, more technical errors, a decrease in psychomotor performance, decreases in driving vigilance, and greater lane lateral position deviation were some of the measures reported in these studies. Dehydration is often associated with exposure to hot environments (Popkin et al., 2010) and whilst it is possible that the thermal conditions may have evoked some level of dehydration which influenced the results observed in these studies, hydration status was not independently considered and therefore at this time it cannot be isolated as an attributable factor in the reduction of driving related performance. Further investigation is required in order to examine the impact of dehydration on driving related skills and performance.

2.2.5 Summary

Water is essential for the human body and needed for virtually all body functions. Fluid intake that balances losses and ensures adequate hydration of body tissues is fundamental for health and life. On average, adults lose approximately two to three litres of fluid each day as a consequence of daily living. Typically, these losses are balanced with water intake from foods and fluids. However, water losses may increase substantially with physical exertion or exposure to thermal environments causing increased perspiration rates. Under these conditions, voluntary fluid intakes do not always match losses and may lead to dehydration. There are multiple methods of determining dehydration level. Assessment of body weight loss following physical activity offers a practical, reliable and accurate measure of dehydration in acute (less than four hours) environments.

Fluid loss can influence cognition. Mild to moderate levels of dehydration can disturb mood and cognitive functioning. Results from several studies reporting the effects of exercise-induced dehydration on cognitive performance (i.e. fatigue, mood, perceptual discrimination, CRT, visual-motor tracking, STM, LTM, attention) suggest that a body water deficit of ~2% BW is sufficient to impair functions and performance. However, results from some studies are ambiguous with inconsistencies reported particularly for mild and moderate levels of dehydration. This may be a reflection of methodological differences between studies including the dehydration protocol, dehydration level and the cognitive task employed. Many studies have induced dehydration through combinations of exercise and heat stress, which make it difficult to interpret the effects of dehydration. Those studies that have attempted to isolate exercise as a dehydration method also have limitations. In most cases, studies had small sample sizes and cognitive tests were completed without sufficient periods of rest following exercise. Thus, a fatigue component may have influenced results. Discrepancies in findings may also be a result of numerous testing instruments that have been used across studies to measure cognitive performance as well as the relative sensitivity of these measures. Cognitive performance decrements invoked by dehydration may be largely dependent on the cognitive task itself, its complexity and the magnitude of processing required to successfully perform the task. Further research examining the effects of dehydration on cognitive performance is required.

2.3 Alcohol

2.3.1 Preface

2.3.2 The Social Context of Alcohol Use in Australia

  2.3.2.1 Alcohol Use Following Physical Activity or Exertion

2.3.3 The Fate of Alcohol in the Human Body

  2.3.3.1 Factors affecting Blood Alcohol Concentration

  2.3.3.2 Measures of Alcohol Concentration

2.3.4 Physiological Effects of Alcohol on the Human Body

  2.3.4.1 Subjective Effects of Alcohol

  2.3.4.2 Effects of Alcohol on the Central Nervous System

  2.3.4.3 Alcohol and Fluid Homeostasis

2.3.5 Effects of Alcohol on Cognitive Performance

  2.3.5.1 Reaction Time

  2.3.5.2 Executive Function

  2.3.5.3 Cognitive Inhibition

  2.3.5.4 Driving Performance

  2.3.5.5 Alcohol Expectancy

2.3.6 Summary

2.3.1 Preface

The acute effects of alcohol on the human body are widespread and can be relatively mild or destructive in nature. The effects of alcohol are expressed in both physiological and psychological domains, and these are often inter-related. These effects vary and depend on a number of factors including the type and quantity of alcohol consumed, the age, weight and gender of the drinker, body chemistry, the conditions of consumption (e.g. with or without food), drinking experience, and the situation in which drinking occurs. A combination of these factors leads to significant individual variability in response to alcohol's effects. In alcohol-related research it is therefore important to understand both the physiological and psychological effects of consumption. It is also important to examine social factors that may influence drinking behaviours. The context in which

drinking occurs may influence the effects experienced and the outcomes associated with acute alcohol consumption. The following section of the literature review examines the physiological, behavioural and social effects of alcohol consumption. The aim of this section is to provide an understanding of factors that influence the effects of alcohol and describe the impact of acute low to moderate alcohol consumption on cognitive performance and human behaviour.

2.3.2 The Social Context of Alcohol Use in Australia

There is little doubt that alcohol consumption plays an integral part in the lifestyle of many Australians. Alcohol is consumed for enjoyment, relaxation and sociability and in most cases is done so with relatively few adverse affects (National Health and Medical Research Council, 2009). A 2011 annual alcohol poll on the attitudes and behaviours of Australians found that alcohol is consumed by 84% of Australian adults. On average, people who consume alcohol do so two days each week (Alcohol Education & Rehabilitation Foundation, 2011). People drink alcohol for a variety of reasons and do so in many different social and cultural contexts. Generally, fluid consumption is driven by physiological mechanisms that regulate thirst in response to body water deficit (Popkin et al., 2010). Although alcoholic beverages may initially contribute to the suppression of thirst (Eisenhofer & Johnson, 1983), there are many other factors that influence choice of alcohol as a beverage (Arnaud, 1998). For example, consumption may be associated with a particular occasion (e.g. a celebration), the social atmosphere, or may be part of an individual's habitual routine (e.g. a drink after work).

Alcohol has been shown to affect psychosocial factors causing changes in behaviour, which may influence risk-taking activities following its consumption (Lane et al., 2004). The disinhibiting effects of alcohol may influence one's inclination to engage in activities that involve greater risk than they otherwise would. The outcomes of which could be unfavourable or even fatal. Alcohol has been shown to influence dangerous and risky driving behaviour (Fillmore et al., 2008). In 1997,

alcohol was linked to over 400 road fatalities and almost 7800 hospitalisations as a result of motor vehicle injuries in Australia (Chikritzhs et al., 1999). More recent data suggests that alcohol is a factor in over 25% of road trauma deaths, 8% of injury crashes and 6% of all motor vehicle accidents annually (Roads and Traffic Authority, 2007). There is also a link between alcohol consumption and increases in other behaviours such as aggression (Taylor & Chermack, 1993), risky sexual behaviour (Testa & Collins, 1997), accident-related injuries (Cherpitel, 1993, 1999) and criminal activity (Lanza-Kaduce et al., 1997).

The Australian guidelines aimed at reducing the risk of alcohol related harm on a single occasion of drinking stipulate that no more than four standard drinks (each containing 10g of alcohol) should be consumed on any one occasion. However, population awareness of these guidelines has been shown to be low, with approximately 10% of people familiar with this recommendation (Alcohol Education & Rehabilitation Foundation, 2011). Many factors other than the volume of alcohol consumed may potentially influence the physiological and subsequent behavioural response to alcohol. The remaining sections of this literature review describe the fate of alcohol in the human body, factors that influence alcohol concentrations achieved in the body and the effects of alcohol consumption on cognitive performance.

2.3.2.1 Alcohol Use Following Physical Activity or Exertion

Alcohol consumption is a common practice amongst individuals following a period of physical activity or exertion. The vast majority of research shows that sport participation, particularly team-based sports, is associated with increased rates of hazardous drinking (Blair et al., 1985; O'Brien & Lyons, 2000; Dunn & Wang, 2003; Martens et al., 2006; Musselman & Rutledge, 2010). This connection is likely related to the fact that drinking is centred on team socialising and bonding (Brenner & Swanik, 2007); events that often occur at a bar or licensed clubhouse associated with sporting venues (Black et al., 1999; Clayton & Harris, 2008). In addition, alcohol

cultures, norms and expectations specific to certain sports, clubs and teams promote this association (Brenner & Swanik, 2007). Furthermore, sporting teams are often sponsored by breweries, microbreweries and bars (Duff et al., 2004). This relationship is often emphasised as many sports clubs rely on alcohol sales to raise revenue (Duff et al., 2004). Accordingly, alcohol and sport are inextricably linked in terms of the social norms and cultures associated with sports, as well as in those of the alcohol industry which funds a variety of sports clubs.

In relation to working environments, industrial workers are among the occupational groups that have the highest proportion of full-time employees that consume alcohol (Zhang & Snizek, 2003). There is some evidence to suggest that adverse occupational working conditions (i.e. working in hot environments etc.) may be partly responsible for this, with workers using alcohol as a coping mechanism for harsh working conditions and to aid relaxation (Zhang & Snizek, 2003). A number of sociological studies have described alcohol consumption among industrial-type workers as being part of the occupational culture (Janes & Ames, 1989; San José et al., 2000; Zhang & Snizek, 2003; Berry et al., 2007).

In some cases alcohol may be consumed after physical activity/exertion that has resulted in fluid loss and where insufficient rehydration has occurred. The consumption of alcohol under conditions of mild or moderate dehydration may influence individuals' willingness to take risks more so than under conditions where fluid deficit is not present. This may result in increased incidences of injury and harm through alcohol mediated risk-taking behaviour (i.e. driving under the influence).

2.3.3 The Fate of Alcohol in the Human Body

The fate of alcohol in the human body has been well documented and refers to a science known as alcohol pharmacokinetics. A number of extensive reviews on this topic are available (Jacobsen, 1952; Westerfeld, 1961; Hawkins & Kalant, 1972; Pawan, 1972; Holford, 1987;

Pohorecky & Brick, 1988; Eckardt et al., 1998; Lieber, 2005). It is important to describe factors that contribute to Blood Alcohol Concentration (BAC), as this is the main determinant that influences human behaviour and performance following alcohol consumption.

Alcohol ingestion results in increased BAC, which reaches a peak level before being eliminated from the body and returning to baseline. The general behaviour of BAC over time follows what is known as the blood alcohol curve, and is presented in Fig. 2.3a. (Pikaar et al., 1988). The peak BAC achieved following alcohol ingestion is subject to many factors. These are primarily associated with the absorption, distribution and elimination of alcohol in the body.
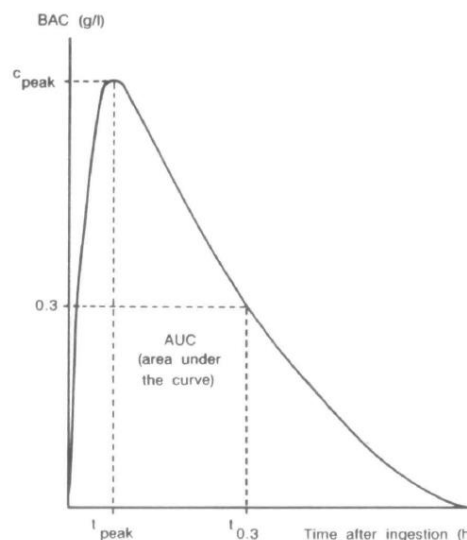
Fig. 2.3a. Blood alcohol curve. Taken from Pikaar et al., (1988).

Alcohol is both water and lipid soluble, and can be absorbed chemically unaltered along the entire length of the gastrointestinal tract by passive diffusion (Pawan, 1972). Typically, only a small amount of alcohol is absorbed directly from the stomach (10-20%) (Pawan, 1972; Pohorecky & Brick, 1988), with the majority taking place in the small intestine (Pohorecky & Brick, 1988; Eckardt et al., 1998; Roberts & Robinson, 2007). The rate at which alcohol is absorbed from the stomach and small intestine contributes most significantly to the amount of alcohol that appears in the

systemic circulation and thus in the CNS (Eckardt et al., 1998). This rate can vary considerably with peak BACs usually occurring 30-90 min following alcohol ingestion (Pohorecky & Brick, 1988).

Following absorption, alcohol is distributed throughout the body compartments via the circulatory system. This process is complex and does not occur uniformly throughout the body. Because it is water soluble, alcohol rapidly infiltrates tissues that have greater blood supply and water content (Pohorecky & Brick, 1988). It is therefore not surprising that alcohol is rapidly distributed to tissues such as the brain, which has both high water content and a rich vasculature network. Variation in tissue matter and subsequent water content between individuals may impact on the peak alcohol concentration attained following ingestion and provides some explanation for the differences observed between individuals. Elimination of alcohol from the body principally occurs through metabolism, with only small amounts excreted in the breath (0.7%), urine (0.3%), and sweat (0.1%) (Holford, 1987).

Alcohol metabolism begins well before absorption is complete (Pohorecky & Brick, 1988). Initially, metabolism does not keep pace with absorption, which accounts for the increase in BAC observed following consumption (Miles, 1922). Once ingestion has ceased and BAC peaks, alcohol is slowly eliminated from the body, resulting in a complete disappearance of alcohol from the blood. Numerous chemical processes are involved in the metabolism of alcohol, beginning with the oxidation of alcohol to acetaldehyde. A series of reactions then take place to metabolise acetaldehyde to acetic acid and finally to water and carbon dioxide (Pawan, 1972). The most important of these steps is the initial reaction, which is often referred to as the rate-limiting step (Pawan, 1972). Three separate metabolic pathways (Alcohol Dehydrogenase (ADH), Microsomal Ethanol Oxidising System (MEOS), and Catalase) have been identified, which facilitate the initial oxidation of alcohol to acetaldehyde. Each is based on the enzyme that catalyses the reaction in particular cell compartments of the tissue. Alcohol dehydrogenase activity occurs both in the stomach and liver, whilst MEOS and catalyse activity occurs primarily in the liver. A number of

41

extensive reviews on the pathways of alcohol metabolism are available (Jacobsen, 1952; Hawkins & Kalant, 1972; Pawan, 1972; Crabb et al., 1987; Lieber, 2005). The time required for both peak BAC levels and complete elimination to occur is remarkably variable between individuals and may partly be explained by factors influencing rates of alcohol metabolism.

2.3.3.1 Factors affecting Blood Alcohol Concentration

Blood alcohol concentrations achieved after drinking are subject to a combination of factors that influence the absorption, distribution and metabolism of alcohol (Pohorecky & Brick, 1988; Eckardt et al., 1998). The most significant factor to affect BAC is the dose of alcohol consumed. Given the same dose of alcohol, blood alcohol curves would vary considerably between individuals (O'Neill et al., 1983). Thus, summarising the findings from studies that have used vastly different approaches to investigate the effects of alcohol is complicated. The use of absolute dose (i.e. set number of drinks) versus relative dose (i.e. as a function of body weight) protocols makes interpretation of findings between studies difficult, particularly with the variability in alcohol response between individuals of different body size, weight and gender, and under different administration practices (i.e. with or without food, volume and type of beverage, timing of ingestion etc.). The high degree of variability in response to both absolute and relative doses of alcohol highlights the need for close attention to be given to alcohol administration procedures.

Several studies have employed methods that predict required doses of alcohol in order to achieve a target BAC (Liu & Fu, 2007; Roberts & Robinson, 2007; Guillot et al., 2010). These methods are based on calculations using an algorithm developed by Widmark in 1932 (Widmark, 1981), which describes the relationship between alcohol ingestion, the alcohol concentration in blood and body weight. An updated version of this algorithm, which factors in the total body water content of individuals has been developed more recently (Watson et al., 1981). Peak BAC levels achieved in studies using standardised dosing protocols accounting for individual

characteristics such as age, gender, height, weight and total body water content, appear to produce more consistent results. Future investigations into the effects of alcohol should therefore employ methods to individually calculate doses for target BACs.

Absorption

Several factors influencing the rate of alcohol absorption in the gastrointestinal tract are thought to contribute to the variability observed in BAC levels. These primarily include alcohol concentration (Miles, 1922; Lolli & Rubin, 1943; Pohorecky & Brick, 1988; Roine et al., 1991; Roberts & Robinson, 2007) and the type of alcoholic beverage consumed (Newman & Abramson, 1942; Roine et al., 1993; Franke et al., 2004). There is also some evidence suggesting differences in the level of carbohydrates and congeners (Haggard et al., 1943; Marczinski & Stamates, 2013), carbonation of the beverage (Roberts & Robinson, 2007), and experimental manipulations such as alcohol expectancy (Collins et al., 1996; Cole-Harding & Michels, 2007) may influence alcohol absorption rates, increasing first-pass metabolism and ultimately reducing BAC levels. However, limited studies have been completed on these variables and further research is needed to confirm these observations.

Distribution

The primary factor influencing distribution is the rate at which alcohol is absorbed from the gastrointestinal tract and infiltrated into the circulatory system. However, as alcohol quickly equilibrates with body water, individual TBW content can also influence the rate of alcohol distribution in the body. Total body water is a function of a person's age, gender, body weight, and body composition. Higher TBW content is generally found in younger individuals who are male, have greater body weight and a higher proportion of lean body mass. Comparing gender differences in alcohol pharmacokinetics, Goist et al., (1985) provided a group of males and females

43

with doses calculated for body weight and total body water. Women reached significantly higher peak BACs than men when given equivalent doses of alcohol based on body weight. However, when provided with doses based on estimated total body water, no differences in peak BACs between genders was observed. In addition, peak BACs in women were significantly lower when the dose was based on body water compared to body weight, whilst there was no difference observed between administration models in men.

Greater body weight provides a greater volume in which alcohol can be distributed, suggesting that larger individuals may be less affected by a given amount of alcohol. Alcohol is also more soluble in water than in fat (Paton, 2005) and is therefore distributed more widely in individuals with less fat mass (Marshall et al., 1983). Females and older individuals generally have a smaller body mass and a higher proportion of body fat, contributing to lower TBW content in which to distribute alcohol (Vogel-Sprott & Barrett, 1984; Mumenthaler et al., 1999). In this case, these groups generally exhibit higher BACs than males and younger individuals after consuming the same amount of alcohol (Marshall et al., 1983; Lucey et al., 1999; Mumenthaler et al., 1999).

The relationship between alcohol and total body water content suggests that hydration level may influence BAC. Hydration level is acutely variable in individuals (Shirreffs, 2009) and many people consume alcohol after a period of physical activity or exertion that results in fluid loss through sweating (e.g. after a sporting match or hard physical labour). The consumption of alcohol under conditions of mild or moderate dehydration may result in changes to alcohol's pharmacokinetic profile compared to conditions where fluid deficit is not present. However, the influence of fluid loss through sweating on alcohol pharmacokinetics is yet to be investigated.

Metabolism

Alcohol metabolism varies significantly amongst individuals. On average, moderate drinkers metabolise and eliminate alcohol at a rate of approximately 0.015% per hour. However, this rate

can vary between 0.010-0.034% per hour (Pohorecky & Brick, 1988). The metabolism of alcohol is dependent on the activity of the alcohol metabolising enzymes, specifically in the ADH and MEOS pathways. At relatively low blood alcohol concentrations, ADH enzyme activity accounts for the majority of alcohol metabolism (Crabb et al., 1987). However, large doses of alcohol saturate the ADH enzymes and increase MEOS activity, which can increase the rate of alcohol metabolism (Mumenthaler et al., 1999). Genetic and ethnic differences between individuals have been shown to affect the rate of alcohol metabolism. The vast array of ADH iso-enzymes seen between different genetic and ethnic groups can influence the rate of alcohol elimination (Ramchandani, Bosron, et al., 2001; Lieber, 2005). Individuals with a greater concentration of iso-enzymes with high kinetic properties metabolise alcohol more rapidly, resulting in reduced BAC levels. Likewise, lower gastric ADH activity in females compared to males may account for gender differences in alcohol metabolism (Frezza et al., 1990; Baraona et al., 2001). Lower gastric ADH activity results in less first pass metabolism of alcohol and may contribute to higher BACs in women compared to men provided with the same dose of alcohol (Mumenthaler et al., 1999).

A number of studies have also confirmed the effect of meals and meal composition on rates of alcohol metabolism and peak BAC levels (Southgate, 1925; Lin et al., 1976; Sedman et al., 1976; Welling et al., 1977; Shultz et al., 1980; Schmidt & Oehmichen, 1985; Pikaar et al., 1988; Jones et al., 1997). The consumption of food impacts on the metabolism of alcohol by manipulating gastric emptying rates and allowing more time for alcohol to be metabolised by the gastric ADH enzymes. Effectively, this results in lower and delayed times to peak BAC (Pohorecky & Brick, 1988).

2.3.3.2 Measures of Alcohol Concentration

Traditionally, samples of venous blood have been collected and analysed for the medico-legal diagnosis of alcohol intoxication (Haggard et al., 1940). However, the introduction of the motor

vehicle posed implications for measuring intoxication through blood sampling at the roadside and created a need for alternative methods of alcohol intoxication screening (Holcomb, 1938).

Based on the understanding of respiratory physiology, which assumed a direct correlation between the concentration of alcohol in the alveolar air and concentration of alcohol in the blood, the first record of using breath samples to estimate BAC was conducted by Bogen (1927). However, it was several decades later that a practical device for measuring breath alcohol concentration (BrAC) at the roadside was invented (Hlastala, 1998). Many studies have since attempted to quantify the relationship between BrAC and BAC (Harger et al., 1950; Jones, 1978; Emerson et al., 1980; Simpson, 1989; Jones & Andersson, 1996, 2003). These studies indicate a surprising level of variability in measures using breath analysis (Mason & Dubowski, 1976; Jones, 1978; Emerson et al., 1980). To this day, there is still a limited understanding of the breath alcohol test and its limitations (Hlastala, 2010). As such, alcohol concentration of blood sampling remains the 'gold standard' for determination of alcohol intoxication level. However, when practicality is required, breath alcohol measures provide a relatively accurate and viable alternative. Understanding the relationship between measures from BrAC devices and blood measures is important, particularly where analysis leads to the prosecution of individuals for driving under the influence of alcohol at or near statutory alcohol limits.

2.3.4 Physiological Effects of Alcohol on the Human Body

The physiological effects of alcohol on the human body have been well documented (Pohorecky & Brick, 1988; Eckardt et al., 1998). The acute effects of alcohol are familiar to most people and many individuals consume low doses of alcohol to induce positive moods, to reduce stress and tension and to promote social interactions (Davidson et al., 1997). The moderate consumption of alcohol has also been associated with health benefits, including reductions in cardiovascular morbidity and mortality (Meister et al., 2000). It is beyond the context of this thesis to discuss the

health benefits and implications of alcohol consumption. However, it is important to discuss the effects of alcohol that may translate to influences on cognitive function. Alcohol is known to have physiological effects on the central nervous system, specifically through neurotransmitter interactions (Deitrich et al., 1989). Alcohol is also commonly reported to have diuretic properties, promoting increased urine output that may encourage fluid imbalance and dehydration (Eggleton, 1942). This section of the literature review will examine the physiological effects of alcohol on the human body, firstly describing the subjective effects of alcohol, followed by a brief discussion of the effects alcohol has on the central nervous system. Finally, the influence of alcohol consumption on fluid homeostasis will be examined.

2.3.4.1 Subjective Effects of Alcohol

Alcohol is often classified as a general CNS depressant (Eckardt et al., 1981) and the sedative action of alcohol is often described using self reported measures of the subjective effects and through the monitoring of electroencephalography (EEG) activity patterns (Martin et al., 1993). There is also evidence suggesting that alcohol has transient stimulatory properties, especially at low to moderate blood alcohol levels (Pohorecky, 1977; Martin et al., 1993). This has prompted what is known as the biphasic actions of alcohol.

Several studies have examined the proposed biphasic effects of alcohol (Pohorecky, 1977; Martin et al., 1993; Holdstock & de-Wit, 1998; King et al., 2002). In the development and validation of a biphasic alcohol effects scale, Martin et al., (1993) had 42 social drinkers complete a 14-item stimulant and sedative sub scale questionnaire during the ascending and descending limbs of their alcohol curve. Participants consumed 0.75 ml/kg (males, n=30) or 0.65 ml/kg (females, n= 12) of absolute alcohol in 15-20 min and completed the subscales when BAC was rising between 0.03% and 0.06% and then again at the same BAC level on the descending curve. The authors found that scores for stimulant subscales were higher during the ascending limb compared to the

descending limb, with the opposite response true for the sedative subscale. This suggests that using alcohol concentration alone to explain alcohol's effects is insufficient and that the direction of alcohol concentration is important. Furthermore, acute subjective responses to alcohol may be an important determinant in explaining individual differences in alcohol associated effects.

To examine individual variations in biphasic effects, Holdstock et al., (1998) evaluated the subjective and behavioural effects of alcohol across a range of doses in social drinkers. Forty-nine participants consumed 0.2, 0.4, or 0.8 g/kg of alcohol over a 10 min period prior to having subjective and behavioural responses assessed at regular intervals over three hours. Results indicated that the lowest dose of alcohol (0.2g/kg) had no effect on ratings of stimulant-like or sedative-like effects, and the 0.4 g/kg dose only produced sedative-like effects during the descending limb of the alcohol curve (90 min post ingestion). On the other hand, the high dose of alcohol (0.8 g/kg) produced both stimulant-like and sedative-like effects during the ascending limb (30 and 60 min post ingestion), and only sedative-like effects during the descending limb (90 and 180 min post ingestion) of the alcohol response curve. These findings challenge the assumption that alcohol has biphasic effects, particularly at low doses, and suggests that significant, robust individual differences exist in the subjective responses to alcohol.

A more recent study by King et al., (2002) examined the biphasic response of alcohol in heavy and light drinkers using the same subscale measures as Martin et al., (1993). Thirty-four participants, 14 of whom were considered light drinkers (≤5 drinks per week) and 20 heavy drinkers (≥10 drinks per week) were given 0.4 or 0.8 g/kg of alcohol to consume over 15 minutes. Subjective measures of alcohol effects were then collected at 15, 45, 105 and 165 min post alcohol ingestion. Heavy drinkers were more sensitive to the stimulant effects of alcohol during the ascending limb with the high alcohol dose and showed lower sedative effects with both alcohol doses during the descending limb of the alcohol curve compared to light drinkers. It was also noted that light drinkers did not have a biphasic response to alcohol, with no increase in

stimulation and heightened sedation in both limbs of the alcohol response curve for both doses consumed. This suggests that individual differences in subjective responses to alcohol may be dependent on patterns of alcohol use. The development of a tolerance to the sedative effects of alcohol proposes an explanation for the stimulatory effects reported with high alcohol doses in some people.

2.3.4.2 Effects of Alcohol on the Central Nervous System

The effects of alcohol on the CNS are complex (Mitchell, 1985). Generally, alcohol is reported to have a profound effect on the cells of the CNS resulting in neurobehavioural changes that influence emotional state, sensory function and cognitive performance (Stritzke et al., 1995; Fillmore, 2007; Oscar-Berman & Marinkovic, 2007). In fact, it is often assumed that individuals consume alcohol in order to experience some of these CNS effects (Eckardt et al., 1998).

Specific regions of the brain are selectively vulnerable to the acute effects of alcohol (Lee et al., 2009), particularly the cerebral cortex, limbic system, and the cerebellum (Moselhy et al., 2001; Oscar-Berman & Marinkovic, 2003; Sullivan, 2003). Collectively, these regions of the brain control many functional activities and are involved in cognitive processing, motor control, memory, and the expression of emotions and mood state (Marieb & Hoehn, 2007). When consumed, alcohol is freely available to interact with these brain regions. Acute alcohol consumption can have both subtle and dramatic effects on the brain and affects various parts of the brain in different ways. The mechanism(s) by which alcohol exerts its effects on the CNS have been documented in several reviews (Deitrich et al., 1989; Valenzuela, 1997; Eckardt et al., 1998) and will be briefly described here.

Mechanism of Action

The actions of alcohol on the brain are most likely due to its diverse effects on synaptic transmission involving a variety of neurotransmitters (Watson & Little, 2002). However, evidence from Positron Emission Tomography (PET) studies also suggest that alcohol influences cerebral blood flow, particularly to the cerebellum and may be partly responsible for disruptions in functions such as fine motor coordination (Volkow et al., 1988). A number of studies have also suggested that alcohol metabolites (i.e. acetate) have significant pharmacological effects which are separate from the alcohol molecule itself and can account for some of the peripheral effects observed after alcohol ingestion (Carmichael et al., 1988; Orrego, Carmichael, & Israel, 1988; Orrego, Carmichael, Saldivia, et al., 1988; Carmichael et al., 1991). The most well defined mechanism of action on the CNS is thought to occur through the modulation of neurotransmitter actions. Biochemical and electrophysiological experiments have shown that alcohol alters the function of a large variety of receptors, ion channels, transporters and second messenger systems (Deitrich et al., 1989).

Neurotransmitter Effects

When alcohol interacts with the cells of the CNS it alters the balance between inhibitory and excitatory neurotransmission. More specifically, alcohol has been shown to suppress excitatory nerve pathway activity and increase inhibitory nerve pathway activity (Valenzuela, 1997). Among other actions, alcohol enhances the effects of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA) and abates the effects of the excitatory neurotransmitter glutamine (Faingold et al., 1998). The combined effects of GABA augmentation and glutamine inhibition may induce feelings of drowsiness and lethargy. Alternatively, acute alcohol consumption has been shown to increase dopaminergic neurotransmission (Eckardt et al., 1998). An increase in

dopamine release and turnover may explain the mild euphoria and stimulation of behaviour that is observed in some people following alcohol consumption (Mukherjee et al., 2008).

The effects of alcohol appear to be remarkably varied amongst individuals, and some research shows that neurotransmitter and receptor responses are different across brain regions and under certain experimental conditions (Valenzuela, 1997). Examining the functional states of the main neurotransmitter systems in the brain, Lelevich et al., (2010) found that the expression of neurotransmission was dependent on the alcohol concentration administered. The authors gave rodents either 1, 2.5, or 5 g/kg of alcohol and noted that the low alcohol dose caused no change in neurotransmitter content, whereas the moderate and high doses resulted in prominent changes in the brainstem, thalamus and neo-cortex. In addition, the moderate dose alterations were observed in the key transmitters of the catecholaminergic system, with decreases in dopamine and norepinephrine. On the other hand, the high alcohol dose resulted in increased levels of GABA, showing a prevalence of inhibitory processes. Dopamine and norepinephrine levels, however, were less expressed in the high dose compared to the moderate dose.

It has been suggested that important genetic components may be responsible for the variations seen in individual neurotransmission differences. Researchers have used animal models to scan genomes and identify genes whose activity differs among those that respond differently to alcohol (Crabbe et al., 1999; Liang et al., 2003). Among many of the other responses, it is likely that individuals who become sleepy or sluggish soon after drinking experience a greater effect of alcohol on the GABA neurotransmitter pathways. Alternatively, individuals who become lively and excited following alcohol consumption may have greater dopaminergic responses. Differences in neurotransmitter activity may also be a result of previous alcohol exposure (Browman & Crabbe, 1999; Schuckit et al., 2004).

Clearly, mechanisms related to neurotransmitter activity and receptor function provide some explanation for the effects of alcohol throughout the body, particularly via CNS effects. However,

51

further research is required to better understand the genetic and environmental characteristics that contribute to the marked interpersonal variability in response to alcohol consumption.

2.3.4.3 Alcohol and Fluid Homeostasis

The diuretic potential of alcohol has been known for decades with early studies observing increased urine output following the ingestion of alcohol compared to water (Murray, 1932; Eggleton, 1942). Most investigators agree that alcohol diuresis is probably due to inhibition of the anti-diuretic hormone arginine vasopressin from the pituitary gland (Murray, 1932; Eggleton, 1942). However, there is some evidence to suggest that this may not be the only mechanism of alcohol induced diuresis and alcohol may also act directly on renal tubular re-absorption (Linkola et al., 1978; Taivainen et al., 1995).

Given the known diuretic effects of alcohol, it is often suggested that consumption of alcohol-containing beverages should be avoided when fluid replacement is required. However little evidence supports this notion (Shirreffs & Maughan, 1997). To investigate the diuretic properties of alcohol further, Shirreffs & Maughan (1997) examined the effects of alcohol on the restoration of fluid balance in dehydrated individuals. After exercise induced dehydration of 2% BW loss, participants were provided with a drink containing 0, 1, 2, and 4% alcohol in a volume of fluid equivalent to 150% of BW loss during exercise. Urine production increased with larger quantities of alcohol but they were not different between trials except for the 4% alcohol beverage, which showed increased urine output up to six hours post ingestion compared to the other drinks. Plasma vasopressin concentration did not differ between trials at any time, although showed a trend for increased concentrations immediately after dehydration, followed by a sharp decrease after alcohol consumption. These values were only significantly different in the high alcohol drink. Overall, the results from this study suggest that alcohol has little diuretic effect in dehydrated individuals, particularly if a sufficient volume of fluid is consumed and the beverage contains no

more than 2% alcohol. There were, however, only six participants in this study and the entire volume of fluid (~2155ml) was consumed over 60 min, which may have caused a greater urine output. Perhaps if the same volume of fluid was consumed over a longer rehydration period and more subjects were examined, outcomes may have been different.

More recently, Hobson & Maughan (2010) examined the effect of consuming a dilute alcohol solution on the urine production of individuals under different hydration states (dehydrated or euhydrated). Participants were dehydrated by 1.9% BW loss before receiving water (2% of initial body weight) or no fluid to consume overnight. The following morning, each participant was given one litre of beer (4% alcohol v/v) to consume in 30 min and urine volumes were collected for four hours after ingestion. A significantly greater urine output was observed during the euhydrated trials compared with the dehydrated trials, suggesting that the diuretic action of alcohol is diminished when individuals are in a state of negative fluid balance.

A very recent study by Desbrow et al. (2013) investigated the effect of manipulating the alcohol and sodium content of beer on fluid restoration following exercise. Participants were dehydrated by ~2.0% body mass before consuming low alcohol beer (2.3% alcohol), low alcohol beer with 25 mmol/L of added sodium, full strength beer (4.8% alcohol), or full strength beer with 25 mmol/L of added sodium over four different trials. Participants consumed volumes of beer equivalent to 150% of body mass loss over a 1hr rehydration period. Net fluid balance was significantly enhanced following consumption of the low alcohol beer with 25 mmol/L of added sodium compared to the full strength beer treatments, which was primarily due to significantly lower accumulated urine output. As a collective, these findings demonstrate the need for further investigation on the diuretic effects of alcohol, and use of alcohol beverages as a rehydration agent.

2.3.5 Effects of Alcohol on Cognitive Performance

An extensive amount of literature exists describing the effects of alcohol on a variety of cognitive skills (Moskowitz & Fiorentino, 2000). The general consensus with regard to its effect indicates that the magnitude of impairment observed occurs in a dose-response manner (Moskowitz & Robinson, 1988). However, not all aspects of performance are equally sensitive to the impairing effects of alcohol and this is especially true with low or moderate doses (Mitchell, 1985). In addition, the level at which significant impairment is observed depends on factors such as the type and complexity of the cognitive task performed (Ogden & Moskowitz, 2004). Cross-study inconsistencies and variations in research methodology (e.g. type of task, alcohol administration and dosage, time of testing, dietary standardisation, gender) as well as the inter-individual and inter-occasional differences in the effects of alcohol on cognitive performance have added to the inconsistent findings throughout the literature. This makes it difficult to provide definitive conclusions regarding the effects of low to moderate doses of alcohol on cognitive performance.

The following section will review the literature investigating alcohol and cognitive performance. Specific isolated tasks including reaction time, executive function and cognitive inhibition are discussed. Furthermore, as this thesis is focused on the effect of dehydration and alcohol consumption on cognitive function and human performance, the applied task of driving a motor vehicle has been chosen for review to examine the impact of alcohol consumption in this context. Only studies that have reported BAC levels ≤0.10% have been included in order to limit the review to studies using low to moderate alcohol doses.

2.3.5.1 Reaction Time

Some of the earliest studies examining the effects of alcohol on cognitive performance were completed using attention tasks, particularly simple (SRT) and choice (CRT) reaction times

(Warren, 1887; Benedict, 1916; Miles, 1916, 1924). A number of reviews of the early work on alcohol found that moderate doses of alcohol were consistently associated with increased reaction times (Jellinek & Jolliffe, 1940; Jellinek & McFarland, 1940; Carpenter, 1962). However, many of the studies included in these reviews were also criticised for being low in quality and having poor sophistication (Carpenter, 1962). This is primarily attributed to low sample sizes, poor procedural control and the inability to apply systematic routine in testing.

Studies using SRT experiments have shown less consistency in their findings of alcohol-induced impairment compared to more complex reaction tasks. This is probably because the experiments involve repetitive testing under single stimulus-response conditions, where there is a much greater likelihood in predicting responses. Based on this premise, many authors consider SRT an insensitive measure of cognitive attention (Moskowitz & Fiorentino, 2000; Ogden & Moskowitz, 2004). Reaction time tasks that involve multiple stimuli and response possibilities provide a greater information processing load than SRT tasks (Moskowitz & Robinson, 1988). Choice reaction time tasks have therefore been somewhat more consistent in revealing impairment following alcohol consumption (Moskowitz & Fiorentino, 2000). In a meta-analysis on alcohol and reaction time, Maylor & Rabbitt (1993) demonstrated that doses of 0.8 and 1.0 ml/kg BW produced a consistent slowing of reaction time on CRT tasks, and did so in a linear manner regardless of the complexity of the task (i.e. 2, 4, 8 choices). Based on these results, the authors proposed a general linear function to predict the effects of alcohol on reaction time as being $RT_{alcohol} = 1.12RT_{no\ alcohol} - 17.85$, and is indicated in Fig. 2.3b.
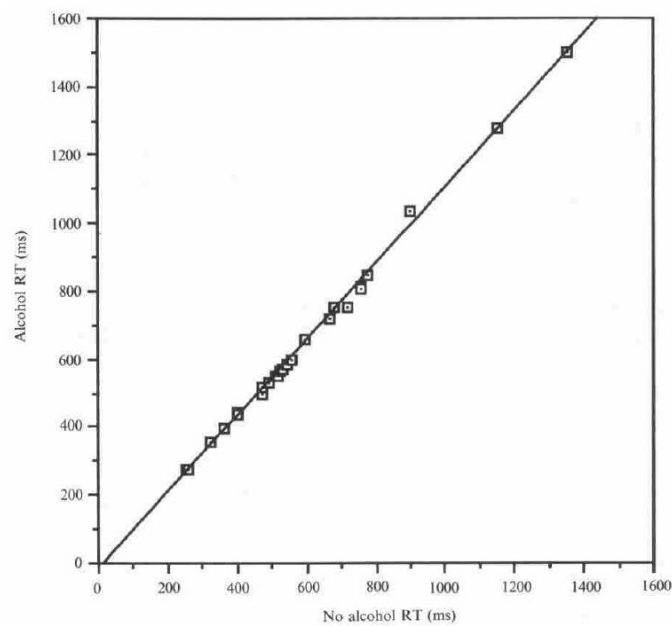
Fig. 2.3b. Mean correct reaction times with alcohol plotted against mean correct reaction times with no alcohol. Taken from Maylor & Rabbitt (1993).

It is important to note that the studies used to conduct this meta-analysis provided relative doses of alcohol and that BAC levels across the studies ranged from 0.067% to 0.099%, including large variability across subjects with standard deviations of approximately 0.020%. In the review of Moskowitz & Fiorentino (2000) the authors reported inconsistent results for the effects of alcohol on CRT across a range of BACs. In 30 tests from 15 studies, 14 found no alcohol impairment and 16 reported an alcohol induced deterioration of CRT at BACs ranging from 0.010% to 0.079%. The lowest BAC where impairment was reported was at 0.020% (MacArthur & Sekuler, 1982), however some studies still reported no impairment on CRT even at BAC levels between 0.060% - 0.063% (MacArthur & Sekuler, 1982; Millar et al., 1992; Finnigan et al., 1995). Above BACs of 0.060%, alcohol had a more consistent impairing effect on CRT and by 0.080% more than 80% of studies showed CRT impairment. The inconsistency in findings across studies was suggested to be associated with the variety of experimental methods employed to measure these effects. However, results from these studies suggest that even the use of CRT as a measure for examining the effects of low to moderate alcohol doses does not always result in measurable deteriorations in cognitive performance.

One other possible explanation for the inconsistent results observed when examining the effects of alcohol on reaction time may relate to the design of assessment tasks that track single indices of performance (Maylor et al., 1987). Reaction time in isolation may not be sufficient to monitor the effects of alcohol, and joint measurements of speed and accuracy allow different aspects of performance to be examined simultaneously (Jennings et al., 1976; Maylor et al., 1987). A study by Maylor et al., (1987) examined the effects of a low alcohol dose (0.33 ml/kg) on speed and accuracy in a CRT task. In 36 participants (18 male, 18 female), the mean BAC achieved with the dose was 0.029% and while the authors found no effect of alcohol on speed, they observed improved accuracy (18.8%) on the CRT task. A paradox with large alcohol doses (1.0 ml/kg) was also observed, where no effect was seen on accuracy, however an increase in reaction time occurred. Similar results were reported by Shillito et al., (1974) who found no effect of alcohol (0.26 ml/kg, BAC = ~0.011%) on reaction time, but observed reduced error rates on a CRT task compared to placebo. Collectively, these results suggest that alcohol may cause an individual to trade-off between speed and accuracy on a task. That is, allow performance on one aspect to diminish, whilst retaining or improving the other. This highlights the importance of considering both speed and accuracy as dependent variables in CRT experiments (Jennings et al., 1976).

2.3.5.2 Executive Function

Executive function (EF) refers to complex cognitive processing that involves the capacity to govern self-directed behaviour (Pihl et al., 2003). It includes tasks such as planning, decision making, problem solving and behaviour inhibition, and is reliant on incoming information from the external environment (Elliott, 2003). Alcohol has been shown to affect performance on tasks associated with EF, particularly with intoxicating doses (BACs of ~0.100%) and under chronic conditions of use. However, little is known about the effects of acute low and moderate alcohol consumption on EF (Guillot et al., 2010). Measures of EF following acute alcohol consumption have

typically been conducted using a number of different laboratory based instruments. These include the Trail Making Test (TMT), Wisconsin Card Sorting Test (WCST) and Tower of London test (TOL) also known as the Stockings of Cambridge test (SOC). However, mixed results have been reported across many of these tasks (Guillot et al., 2010).

Using the WCST, Lyvers & Maltzman (1991) had 10 male and 10 female social drinkers that were either randomly assigned to a placebo or an alcohol beverage targeting a peak BAC of 0.050% complete the task. The authors reported that alcohol intoxicated participants displayed an increase in perseverative errors compared to the placebo group. Using a slightly higher dose of alcohol (mean BAC = 0.059%), Weissenborn & Duka (2003) administered a 0.8 g/kg dose of alcohol to 48 participants (24 male, 24 female) prior to them performing a TOL task using the Cambridge Neuropsychological Test Automated Battery (CANTAB). Results on the task were compared against a group of 47 participants (22 male, 25 female) who received a placebo beverage. Alcohol caused impairment in EF compared to the control group as seen by a decrease in the number of trials completed in minimum moves, as well as an increase in initial thinking time and subsequent thinking time latencies to perform moves. The results of this study support the earlier work of Lyvers and Maltzman (1991) suggesting that the acute administration of a moderate dose of alcohol impairs executive function.

More recently, Guillot et al., (2010) examined the effects of different alcohol doses associated with target BACs of 0.000%, 0.050%, 0.075%, and 0.100% on the EF of males and females using both the WCST and TMT tasks. One hundred and eighty five participants (91 females, 94 males) completed the study following a four hour fasting period. Participants were randomly assigned to one of the alcohol doses and completed the EF tasks 10 min after drinking the beverage. Participants who received either the medium or high alcohol dose had impaired performance on the WCST and TMT tasks compared to placebo. This was determined by an increase in perseverative errors in both groups and an increase in total errors on the task for the high alcohol

dose group. Participants who received the low alcohol dose experienced no significant impairment on the WCST task and displayed improved performance (faster completion) on the TMT task post alcohol consumption compared to baseline performances. In comparison to previous studies examining the effects of alcohol on EF, results from this study suggest some uncertainty and inconsistency in the effects of low alcohol doses on EF performance measures.

Whist the evidence is still limited, acute alcohol consumption in low to moderate amounts appears to have a detrimental effect on EF. There is some inconsistency in findings based on alcohol dose and the BAC at which impairment in EF occurs. However, this may be a result of cross-study differences in methodology including differences in alcohol administration, the type of EF task employed and the use of non cross-over study designs in which inter-individual differences are not able to be controlled for. Further research into the effect of acute alcohol consumption on executive functioning is required.

2.3.5.3 Cognitive Inhibition

Cognitive inhibition is the stopping or overriding of a mental process, in whole or in part, with or without intention (MacLeod, 2007). It is associated with executive functioning and often measured under conditions of alcohol intoxication using response inhibition tasks such as the Stroop, stop-signal, go/no-go, and GoStop tasks (Guillot et al., 2010). The intent of these tasks is to measure an individual's ability to inhibit a pre-potent response to a stimulus. The inhibition of behaviour is an important function that sets the occasion for many other activities requiring self-restraint and regulation of behaviour (Fillmore, 2007). It is often associated with applied tasks which involve complex, goal directed activities such as driving a motor vehicle (Mantyla et al., 2009). For example, an individual may need to inhibit their behaviour whilst driving to avoid contact with an obstacle. Behavioural inhibition is the brain function that prevents us from producing a response no longer suited to the context. Response inhibition tasks allow for

investigation into the impact of alcohol consumption on response inhibition performance. This is typically shown through an increased failure to inhibit responses to no-go or stop targeted stimuli.

During the past decade, laboratory studies have supported the assertion that alcohol consumption impairs basic inhibitory mechanisms (Fillmore et al., 2008). Evidence stems from studies demonstrating that alcohol in moderate doses (BACs of ~0.060%) causes impairment on the Stroop task (Fillmore et al., 2000) and Stop-Signal or Go/No-Go tasks (Fillmore & Vogel-Sprott, 2000; Abroms et al., 2003; Marczinski & Fillmore, 2003; Fillmore & Weafer, 2004; Fillmore, 2007). On the other hand, studies that have employed the GoStop task have not shown impairment in performance under conditions of moderate to high (BACs of 0.050 - 0.100%) doses of alcohol (Dougherty et al., 2008; Guillot et al., 2010). Collectively, these findings suggest that activities requiring a quick suppression of actions might be particularly vulnerable to the disruptive influences of alcohol. However, the particular test chosen to assess this response may be an important study design consideration.

2.3.5.4 Driving Performance

Driving a motor vehicle could be considered one of the most complex cognitive tasks that the majority of individuals are likely to undertake on a daily basis. Hence it is important to determine the impact of alcohol on driving performance. There are obvious risks with the use of actual road based vehicles to conduct these investigations and driving simulators offer the opportunity to examine all of the skills necessary to operate a motor vehicle without the risk of injury. Technological advancements have also assisted to make these instruments more realistic of the driving experience and multiple measures can be assessed throughout the driving test. High transferability of observations has been reported between driving simulators and actual road based assessments (Lee et al., 2003; Bedard et al., 2010) and many studies have concluded that driving simulators can provide accurate and valid observations of drivers' behaviours and functions

(Wald & Liu, 2001; Lee et al., 2003; Bedard et al., 2010). The detrimental effects of acute alcohol consumption on the cognitive skills related to driving have been well documented (Fillmore, 2007). Alcohol impairs judgement and physical abilities as evidenced by performance impairment on discrete tasks related to driving (Ogden & Moskowitz, 2004) as well as actual driving performance itself (Moskowitz & Robinson, 1988; Moskowitz & Fiorentino, 2000). Some studies have shown that impairment begins at very low alcohol concentrations of 0.01 - 0.02% (Moskowitz & Burns, 1990; Ogden & Moskowitz, 2004), whilst others suggest that there is a threshold effect for alcohol related impairment of 0.05%, and no consistent evidence for impairment at BACs below this level (Mitchell, 1985). In an extensive review of the literature from 1981 through to 1998 on the effects of low doses of alcohol on driving related skills, Moskowitz & Fiorentino (2000) suggested that most people are expected to experience impairment in some driving related skills with BACs of 0.08% or less. As a consequence, evidence from these studies has contributed to the development and application of blood alcohol limits for driving.

Studies specifically using driving simulators have demonstrated the impact of alcohol on a number of core driving skills. Alcohol has an influence on driving precision, evident through increased deviation in lane position, number of line crossings (shoulder and centre lines of the lane boundary), and rate of steering wheel movement (Rimm et al., 1982; Banks et al., 2004; Harrison & Fillmore, 2005; Fillmore et al., 2008; Marczinski et al., 2008). These variables are often used as a measure of safe driving performance and are continuously sampled throughout the driving test.

Alcohol has also been shown to influence driving speed and acceleration (Quillian et al., 1999). The relationship between driving speed, crash risk and crash severity has been well established (Rudin-Brown et al., 2009). However, observations between studies are not always consistent. For example, Fillmore et al., (2008) found that alcohol caused drivers to increase speed and acceleration, whilst several other studies have reported that alcohol has no influence on driving

61

speed (West et al., 1993; Burian et al., 2002; Harrison & Fillmore, 2005; Harrison et al., 2007; Marczinski et al., 2008). This may be the result of methodological differences between studies at the time of driving assessment. For example, Fillmore et al., (2008) included a response conflict for the driving test by providing monetary reinforcement for quickly completing the drive, and this may have influenced the overall results obtained.

Braking reaction time (BRT) and brake onset distance are two other measures of driving performance commonly assessed (Rudin-Brown et al., 2009). These variables can be measured precisely in a simulated environment and allow assessment of driver behaviour to hazardous stimuli. Braking reaction time is a measure of the time taken to apply the brake pedal in response to a stimulus (Shinar, 2007). Brake onset distance is a measure of the distance from the point where the brake is applied to the position of the stimulus (Fillmore et al., 2008). Results from a study by West et al., (1993) indicated that low (BAC = 0.025%) and moderate (BAC = 0.050%) doses of alcohol caused an increase in driving hazard perception latency (2.8 and 3.2 seconds respectively) compared to a no alcohol condition (2.5 seconds). Results in a simulator study by Liguori et al., (1999) support these findings, with alcohol dose-ordered increases in braking reaction time observed in response to random hazardous stimuli. In contrast, alcohol appears to have no effect on brake onset distance (Fillmore et al., 2008).

Driving simulator assessments often also include a measure of incidences where a driver fails to stop at a required stimulus (e.g. stop sign, red traffic light etc.) and any off road or other vehicle impacts that occur throughout the test. Under conditions of alcohol consumption, stopping failures have been shown to increase compared to sober (i.e. placebo trial) driving (Fillmore et al., 2008). Off road and other vehicle impacts are usually infrequent in driving simulator studies (Fillmore et al., 2008). However, there is some evidence showing an increased number of accidents under alcohol conditions compared to placebo (Marczinski et al., 2008).

Driving simulators have continued to advance in their technological capabilities. As such, the sensitivity, reliability and face validity of driving simulators have improved. Today, few would argue against the impairing effects of alcohol on driving performance. The focus of investigations has shifted to other likely scenarios where factors such as sleep deprivation, distraction and drug use are combined with alcohol consumption to examine the effects of these variables on driving performance. At the time of completing this thesis, a review of the published literature since the Moskowitz & Fiorentino (2000) report examining studies from 1999 through to 2013, uncovers 47 original research articles investigating the effect of alcohol with or without additional factors on simulated driving performance. A summary of these studies is provided in Table 2.3.

Whilst there is some degree of conflict in results between individual studies, as a collective these studies generally show that alcohol in combination with other stressors results in a greater detriment to driving performance compared to that of alcohol consumption alone. To date, the effect of dehydration combined with alcohol consumption on driving performance has not been investigated.

Table 2.3. Summary of alcohol related driving performance studies from 1999 through to 2013

Studies	Experimental Condition	BAC Levels	Summary of Findings
(Liguori et al., 1999; Quillian et al., 1999; Hack et al., 2001; Calhoun et al., 2004; Strayer et al., 2006; Meda et al., 2009; Huemer & Vollrath, 2010; Veldstra et al., 2011; Weafer & Fillmore, 2011)	Alcohol	0.03% - 0.10%	Alcohol causes impairment in driving performance on a range of measures. Common observations include an increase in inappropriate braking, fewer appropriate complete stops, increased time to execute turns, increased speed variability, increased low speed collisions, increased number of wrong turns, increased standard deviation of lane position, increased average speed, increased within lane deviation, increased steering rate, increased line crossings, greater braking force, decreased headway.
(Robbe, 1998; Ramaekers et al., 2000; Liguori et al., 2002; Lenne et al., 2003; Ronen et al., 2008; Lenné et al., 2010; Ronen et al., 2010; Downey et al., 2013)	Alcohol + Other Drugs	0.025% - 0.09%	Conflicting results. Some studies report that a combination of alcohol and other drugs (e.g. marijuana, ecstasy, dexamphetamine) exacerbate driving impairment, whilst others report that effects are observed with alcohol alone but no synergistic effects are observed when combined with other drugs.
(Vanakoski et al., 2000; Liu & Fu, 2007; Rakauskas et al., 2008; Allen et al., 2009; Liu & Ho, 2010; Wester et al., 2010; Harrison & Fillmore, 2011)	Alcohol + Distraction	0.02% - 0.10%	Alcohol causes impairment in driving precision. Divided attention exacerbates the impairing effects of alcohol.
(Arnedt et al., 2000, 2001; Horne et al., 2003; Banks et al., 2004; Iudice et al., 2005; Howard et al., 2007; Rupp et al., 2007; Vakulin et al., 2007; Vakulin et al., 2009)	Alcohol + Sleep Deprivation	0.025% - 0.08%	Alcohol and sleep deprivation individually cause impairment on a number of driving measures. A combination of both these factors causes even greater deterioration in performance.
(Marczinski et al., 2008; Marczinski & Fillmore, 2009; Bernosky-Smith et al., 2011)	Alcohol & Binge Drinking	0.08%	Alcohol causes impairment in driving performance. No difference between binge and non-binge drinkers, with both groups showing greater impairment under alcohol.
(Burian et al., 2002; Burian et al., 2003)	Alcohol & Expectancy	0.03% - 0.09%	Alcohol causes impairment in driving performance. Expectancy of receiving alcohol decreases risky driving behaviours. No expectancy of alcohol increases risky driving behaviours.
(Liguori & Robinson, 2001; Howland et al., 2010)	Alcohol + Caffeine	0.07% - 0.10%	Alcohol causes impairment in driving performance. Caffeine has no effect on reducing alcohol related impairment of driving performance.
(Harrison & Fillmore, 2005; Harrison et al., 2007)	Alcohol & Driving Ability	0.07% - 0.09%	Alcohol affects driving performance and reduces driving precision. Individuals with poorer baseline skill level are more affected. Individuals trained in difficult conditions display less affected driving performance when under alcohol.
(Spaanjaars et al., 2010)	Alcohol + Water	0.03%	Alcohol causes an increase in risky driving behaviour. Water has no effect on reducing impaired driving performance.
(Barkley et al., 2006)	Alcohol & ADHD	0.04% - 0.08%	Alcohol causes impairment in driving performance. No difference between ADHD and non-ADHD groups for the effect of alcohol on driving ability.
(Fillmore et al., 2008)	Alcohol + Response Conflict	0.08%	Alcohol causes impairment in driving performance, which is exacerbated by response conflict.

2.3.5.5 Alcohol Expectancy

There is evidence to suggest that the behavioural and cognitive responses to alcohol may be mediated by the expectancy of alcohol consumption and the social stigma surrounding its use (Williams et al., 1981; Rohsenow, 1983; Hull & Bond, 1986; McMillen et al., 1989; Finnigan et al., 1995; Fillmore et al., 1998; Hammersley et al., 1998; Burian et al., 2003). In a meta-analysis, Hull & Bond (1986) found both administered alcohol and the expectancy of alcohol have significant effects on behaviour. However, the effects varied significantly across studies.

In a study investigating the effects of alcohol and alcohol expectancy on cognitive impairment using a rapid information processing (RIP) task, Fillmore et al., (1998) provided participants with alcohol (0.62 g/kg), a placebo beverage masked to appear as alcohol or a control group (no beverage). Participants receiving both alcohol and placebo drinks were told that they were receiving alcoholic beverages. To monitor the expectancy effects of alcohol, participants completed a rating scale between -30 (extremely impair) and +30 (extremely enhance) to report how they expected the beverages would affect their RIP task performance (Fillmore & Vogel-Sprott, 1995). No difference in expectancy ratings was observed between the groups receiving alcohol or placebo, with mean expectancy ratings of -11.3±6.9 (range -25 (extreme impairment) to 0 (no effect)). The effects of expectancy were observed in both alcohol and placebo groups with those expecting more impairment performing more poorly on the cognitive task than those expecting less impairment regardless of beverage consumed.

To examine the effects of alcohol expectancy on a dual tracking and reaction-time task analogous to driving skills, in addition to a CRT task, Finnigan et al., (1995) used a balanced placebo design study providing participants (*n*=90 males) with two different doses of alcohol (calculated for a target BAC of 0.040% or 0.080%) or placebo. They were instructed that they were receiving either alcohol or placebo for each condition. The higher dose of alcohol had significant effects on performance across both tasks compared to the lower alcohol dose and placebo

beverages, with no significant difference observed between the lower dose and placebo. In contrast to the work of Fillmore et al., (1998) participants in this study who expected and received alcohol for the higher dose performed significantly better on the tracking task compared to those that expected placebo but received alcohol. In addition, when alcohol was expected but placebo was received, participants performed worse on the CRT task. The authors noted that all of the groups reported a greater perception of drunkenness following beverage consumption and that expecting alcohol made subjects feel more able to perform, regardless of the drink they had received.

It is also possible that participants compensate for alcohol induced deterioration on cognitive tasks if they are aware that they have consumed alcohol. In a study investigating perceptual-cognitive, fine-motor and gross-motor performance tasks using two different alcohol doses (0.68 and 1.36 ml/kg of 80 proof vodka) and placebo, Williams et al., (1981) demonstrated that participants who received placebo but expected alcohol performed worse compared to those who received and expected placebo. However, when participants expected and received the largest dose of alcohol, task performance was improved on the simpler tasks to a level equivalent to that of participants who received and expected placebo. To explain this the authors suggested that compensatory behaviours may occur in individuals that expect and confirm alcohol consumption through interoceptive intoxication cues, especially on tasks that are of low complexity (Williams et al., 1981).

The effects of alcohol expectancy have also been examined in applied cognitive tasks such as driving simulations. In a relatively early simulation study, Rimm et al., (1982) found no effect of alcohol expectancy on driving behaviour in 44 males provided with alcohol (0.74 g/kg) or placebo. The authors found that alcohol had a debilitating effect on braking and steering ability during a driving task but the belief of alcohol consumption had no effects. However, the measures in this study may not have been sensitive enough to observe effects of expectancy. There is some

evidence suggesting that cognitive effects are most prominent when the targeted behaviour involves a conflict (Marlatt & Rohsenow, 1980) and the effects of alcohol expectancies are typically weak, or non-existent in tasks that are strictly mechanical in nature (i.e. reaction time, braking, steering) (Rimm et al., 1982).

Other studies examining effects of alcohol on driving performance have observed expectancy effects based on participants' individual sensation seeking traits. In one study, McMillen et al., (1989) investigated the effects of alcohol, expectancy and the sensation seeking behaviour of individuals on risk taking behaviour during a simulated driving task. A total of 96 participants were provided with alcohol (1.2 ml/kg) or placebo after being instructed that the drinks either did or did not contain alcohol. Results from this study indicated that individuals with higher sensation seeking behaviours took more risks and low sensation seekers were more cautious in driving when they believed they had consumed alcohol regardless of actual consumption. Contrasting results were reported in a study by Burian et al., (2003) examining the effects of alcohol and expectancy on risk taking during simulated driving. Participants (30 male, 28 female) were administered a sensation seeking scale (Zuckerman, 1994) prior to being provided with alcohol (0.5 g/kg) or placebo and told that they had received no alcohol or a dose equivalent to two to three standard drinks. Participants who both expected and received alcohol had a significantly decreased probability of a risky lane choice compared to when alcohol was neither expected nor received. However, pre-existing sensation seeking traits did not significantly influence the probability of choosing riskier lane options. The findings from this study suggest that the knowledge of dose received may differentially influence the pharmacological effect of alcohol on decision-making (Burian et al., 2003).

Collectively, the results of these studies indicate that alcohol expectancy may contribute to differences in cognitive function when either alcohol or placebo beverages are administered. The expectancy effects of alcohol and subsequent influence on cognitive performance may also be

influenced by the sensation seeking traits of individuals. Thorough study designs should consider the potential for expectancy effects when examining the effects of alcohol on cognitive performance measures. The influence of alcohol expectancy on cognitive performance and risk taking behaviour requires clarification.

2.3.6 Summary

The acute effects of alcohol are familiar to most people and can be pleasant or unpleasant, depending on the circumstances and the volume of alcohol consumed. The general consensus is that alcohol at any BAC level departing from zero has the potential to adversely affect CNS function and subsequently influence behaviour. Alcohol interacts with neurotransmitter systems in the brain, manipulating synaptic transmission and receptor activity. The overall neuro-chemical effects of alcohol, and contribution of any of the potential targets to the intoxicating or behavioural effects of the drug is still not completely understood. This may be due to differences in the techniques applied within studies when researching alcohol, but is also a likely outcome of alcohol's multiple effects on humans and the variability of individual responses to the drug. The effects of alcohol are typically described in a dose-response relationship. These effects are more transparent with large doses of alcohol that elicit higher BACs. However, the response to alcohol varies considerably between individuals and BAC level is influenced by a number of factors affecting the absorption, distribution, metabolism and elimination of alcohol from the body. In this case, BAC levels do not always correlate with the subjective effects experienced by individuals nor do they provide a reliable predictor of alcohol related human behaviour.

The acute effects of alcohol on cognitive performance and behaviour have been well described. Several studies have shown that CRT, EF and response inhibition tasks are impaired with alcohol doses associated with BACs below 0.08%, and impairment in the skills related to driving a motor vehicle are expected with BACs of 0.08% or less. There are, however, some studies that report

contrasting results. The inconsistencies reported in findings across studies is likely to be a result of the heterogeneity of methodological approaches used, with a lack of standardisation of testing methods, instruments and measures clearly visible in a review of the literature. The effects of alcohol on cognitive performance may also be influenced by expectancy in alcohol consumption. A number of studies using placebo-based designs suggest that the expectation of receiving alcohol can result in compensatory mechanisms that cause individuals to perform better on tasks after consuming alcohol. However, these effects appear to be dependent on task complexity, with less compensatory ability available on tasks that require considerable cognitive processing.

Due to the proposed diuretic action of alcohol, its consumption following a period of fluid loss and for the purposes of rehydrating has previously not been recommended. However, many people consume alcohol following a period of physical exertion that results in fluid loss. The impact of alcohol on cognitive performance under these conditions requires investigation.

Chapter Three: Research Framework

3.1 Overview

A review of the literature encompassing the core areas of dehydration, alcohol consumption and cognitive performance has highlighted a number of key research questions yet to be examined. The effects of alcohol on cognitive function and human behaviour (particularly risk taking behaviour) have been well documented. Likewise, there is a growing body of evidence describing the effects of dehydration on cognitive performance. There is still some inconsistency in these findings, which may be a result of the methodological differences between studies. No studies have investigated the combination of dehydration and alcohol consumption and their effects on cognitive performance and human behaviour. Given the potential physiological stress accompanying dehydration and the associated cognitive performance impairments that have previously been shown with fluid deficits at ~2% BW loss, one could speculate that a combination of the two factors would elicit a greater performance burden than either in isolation. As such, research examining the combined effects of dehydration and alcohol consumption on driving performance is required.

Overall, the objective of this thesis was to add to the body of knowledge regarding the effects of both dehydration and alcohol consumption on human performance and behaviour. The themes identified as relevant areas of investigation from the literature formed the basis of this thesis. They have been explored using four separate and main Research Studies (Chapters Five to Eight). Research Study One incorporated a mixed-methods approach to data collection to quantify hydration status and fluid consumption practices in a group of participants, before exploring their perceptions towards rehydration behaviour involving alcohol consumption. The methodological approach adopted for the subsequent Research Studies (Research Studies Two, Three and Four)

primarily centred around quantitative methods, where controlled trials were used to examine specific hypotheses. Controlled, randomised cross-over experimental designs were incorporated in these studies to limit the influence of confounding covariates and inter-individual variability, maximising the validity of the research findings.

Research Studies Three (Chapter Seven) and Four (Chapter Eight) were designed to measure the effects of dehydration and alcohol consumption on cognitive performance across tasks of both a discrete and applied (i.e. driving a motor vehicle) nature. As such the studies involved measuring task performance at designated times across the day. Participants involved in these studies were not permitted to consume any meals during the experimental trials. Studies investigating the impact of Ramadan fasting (12-16hrs) on cognitive function have reported adverse effects of carbohydrate deprivation on cognitive ability (Doniger et al., 2006; Maughan et al., 2010). However, there is some evidence suggesting a lack of effect for short-term fasting on cognitive function (Green et al., 1995) and that consuming an energy-containing snack in the afternoon can have positive effects on cognitive performance tasks requiring sustained attention (Kanarek & Swinney, 1990). To avoid confounding effects that may reduce the impact and our ability to detect changes in cognitive performance associated with dehydration and alcohol consumption, the consumption of meals was avoided.

In addition to the main research investigations of this thesis, four pilot investigations were conducted to improve methodological accuracy, validity and reliability within the main Research Studies (Chapter Four). An overview of the research framework is displayed in Fig. 3. Links between investigations and subsequent Research Studies is also outlined in the figure.

Fig. 3. Overview of Research Studies.

CHAPTER 4

CHAPTERS 5, 6, 7, 8

Pilot Study 1

Development and Effectiveness of a Placebo Beverage Similar in Sensory Properties to an Alcoholic Beverage

Pilot Study 2

Accuracy and Reliability of Breath Alcohol Analysis Following Exercise-Induced Dehydration

Pilot Study 3

Test-Retest Reliability of CANTAB Tasks: Effects of Practice and Time of Day with Brief Test-Retest Intervals

Pilot Study 4

Test-Retest Reliability of Simulated Driving Performance

Research Study 1

Industrial Workers' Hydration: Attitudes, Perceptions and Practices Regarding Post-Shift Alcohol Consumption

Research Study 2

Alcohol Pharmacokinetics and Risk-Taking Behaviour Following Exercise-Induced Dehydration

Research Study 3

The Effects of Dehydration, Moderate Alcohol Consumption, and Rehydration on Cognitive Functions

Research Study 4

The Effects of Dehydration, Moderate Alcohol Consumption, and Rehydration on Simulated Driving Performance

The purpose of the pilot investigations was to test logistics and gather information prior to conducting larger studies, in order to improve research quality and efficiency, and to check the reliability and validity of assessment instruments used. Firstly, evidence suggests that the effects of alcohol on cognitive performance may be influenced by the expectancy of receiving alcohol. Studies using placebo-based designs suggest that expectation can cause compensatory mechanisms that cause individuals to perform differently on tasks after consuming alcohol. In order to examine the expectancy effects of alcohol, it is important to have a placebo beverage in which participants are unable to detect differences compared to an alcohol-containing beverage. The initial Pilot Study was therefore undertaken to develop a placebo beverage that could be used successfully in subsequent studies (Research Studies Three and Four) to measure the expectancy effects of alcohol on performance.

The second Pilot Study was a result of secondary analysis from Research Study Two. Breath alcohol analysis is often conducted at the roadside to determine intoxication levels of motorists using hand held breathalysers. Concerns regarding the accuracy and precision of breathalysers have been noted, with many physiological and analytical variables affecting reliability. Dehydration is one biological factor that may influence the reliability of breath analysis. However, no studies have examined these effects. Therefore, the second Pilot Study was completed to determine the effects of exercise-induced dehydration on the accuracy and reliability of breath alcohol analysis. The breathalyser device examined in this study was to be utilised in subsequent studies (Research Studies Three and Four) under various levels of hydration status. Thus, it was important to determine the accuracy and reliability of the device under dehydrated conditions.

Test-retest reliability of assessment instruments is important in behavioural-based research and is a well-established principle in most areas of psychology. The third Pilot Study examined the test-retest reliability of cognitive tasks from the CANTAB testing instrument. These tasks were to be used in a protocol that required repeated assessments of cognitive performance separated by

several hours in the same day (Research Study Three). Similarly, Pilot Study Four examined the test-retest reliability of assessment measures from repeated driving simulator scenarios. The driving scenario and associated assessment measures were to be employed in the final Research Study of this thesis (Research Study Four).

3.2 Research Objectives and Hypotheses

This thesis had four main objectives. Firstly, it is common to observe people consuming alcoholic beverages after a period of physical exertion that causes fluid loss. Dehydration as a result of physical exertion may influence acute alcohol consumption practices. There is some evidence showing increased alcohol consumption and binge drinking practices in individuals who participate in physical activity compared to their sedentary counterparts (Blair et al., 1985; O'Brien & Lyons, 2000; Dunn & Wang, 2003; Martens et al., 2006; Musselman & Rutledge, 2010). However, no research has explored the attitudes, perceptions and practices of individuals likely to experience fluid loss from physical activity and who willingly participate in acute alcohol consumption. The first objective of this thesis was therefore to:

Determine the hydration status of a population group likely to be involved in daily physical exertion that causes dehydration (i.e. industrial/construction workers) and explore the typical post-work behaviours, attitudes and perceptions towards alcohol consumption.

If dehydration does exacerbate alcohol-induced impairment in cognitive function, an understanding of the attitudes, perceptions and behaviours of individuals who consume alcohol following physical exertion is critically important. It was hypothesised that some individuals of this population group would indicate levels of dehydration following daily physical exertion and consume alcohol as part of post-work behaviour with little or no regard for their hydration status.

Following on from this, if individuals are likely to consume alcohol following a period of acute fluid loss causing dehydration, it would be important to investigate the interaction between dehydration and alcohol consumption on the fate of alcohol in the human body. Many factors have been shown to influence the pharmacokinetic response to alcohol. These are important to consider given that symptoms and subjective effects of alcohol are directly related to BACs. The relationship between alcohol and total body water content suggests that changes in hydration level may also influence BAC. However, the influence of acute fluid loss on alcohol pharmacokinetics and subjective ratings of alcohol-related impairment was yet to be investigated. The second objective of this thesis was therefore to:

Investigate the effects of dehydration on alcohol pharmacokinetics and subjective ratings of alcohol's effects.

It was hypothesised that alcohol pharmacokinetic variables associated with the blood alcohol curve would be significantly affected by dehydration, leading to higher BAC levels and greater ratings of perceived intoxication effects when participants consumed alcohol in a dehydrated state compared to being in a euhydrated state. Given the potential for dehydration to influence alcohol pharmacokinetics and subjective ratings of its effects it would be important to examine the interaction between alcohol and dehydration on cognitive functions. Dehydration and alcohol consumption have individually been shown to influence performance on a number of discrete cognitive tasks (e.g. CRT, executive function and response inhibition). The consumption of a moderate dose of alcohol following a period of physical exertion that results in dehydration may have a significantly higher burden on cognitive processes than these factors in isolation. The alcohol-induced effects on cognitive performance on a number of discrete skills may be

exacerbated when individuals are dehydrated compared to when they are adequately hydrated. Hence, the third objective of this thesis was therefore to:

Examine the effects of dehydration, moderate alcohol consumption, and rehydration on cognitive function using discrete cognitive tasks from the CANTAB.

It was hypothesised that the alcohol induced effects on cognitive performance would be greater when individuals were dehydrated compared to those observed when rehydrated following exercise. If the interaction between dehydration and acute alcohol consumption cause a greater deterioration in performance on discrete cognitive tasks, this is likely to have implications for performance on applied tasks where greater cognitive demand and the application of multiple cognitive domains are required. Driving a motor vehicle is likely to be one of the most challenging and cognitive demanding tasks most people undertake each day. Alcohol is well recognised in causing impairment in driving ability, particularly at or above the statutory driving limit of 0.05%. Acute alcohol consumption has direct implications for the safety of individuals operating motor vehicles. However, until now, it has been unknown whether dehydration exacerbates the alcohol-induced impairment of driving performance when moderate amounts of alcohol are consumed (i.e. BACs <0.05%). Therefore the final objective of this thesis was to:

Examine the effect of dehydration, moderate alcohol consumption and rehydration on simulated driving performance.

It was hypothesised that alcohol induced effects on measures of driving performance would be greater when individuals were dehydrated compared to those observed when rehydrated following exercise.

Overall, research from this thesis endeavours to provide an understanding of the impact that dehydration has on physiological, psychological and pharmacokinetic responses to a moderate dose of alcohol. In particular, it examines and attempts to explain the interactive effects of dehydration and moderate alcohol consumption on cognitive functions from both a discrete cognitive domain and applied performance perspective. In addition, research from this thesis explores attitudes, perceptions and behaviours of individuals likely to experience dehydration and participate in acute alcohol consumption. As a collective, results from this body of research may help to provide a better understanding of factors contributing to alcohol-induced risk-taking behaviour and assist in the promotion of informed policy development aimed at minimising the harms associated with acute alcohol consumption.

Chapter Four: Research Methods: Accuracy, Validity and Reliability

4.1 Preface

Interpretation of findings and determining the impact of observations made during the course of a research study is fundamentally reliant on the quality of instrument measures collected. Key indicators of the quality of a measuring instrument are the reliability and validity of the measures (Kimberlin & Winterstein, 2008). Reliability provides a measure of the extent to which results reflect random measurement error, and validity refers to the extent to which the inferences made from a test are justified and accurate (Atkinson & Nevill, 1998). It is therefore important to use testing measures that are reliable and valid to ensure that observations made reflect more than just random error, and also accurately measure the domains of interest. The purpose of this chapter was to provide an outline of validation work completed to examine the reliability of assessment instruments in preparation for their administration into the main studies discussed in this dissertation.

In total, four pilot investigations were completed. The first study examined the effectiveness of a placebo beverage, designed to be similar in sensory properties to that of an alcoholic beverage. An effective placebo beverage would serve as a control beverage to allow the effects of alcohol interventions to be compared against a valid control in subsequent studies. The second study investigated the influence of hydration status on the accuracy and reliability of alcohol concentrations determined by breath analysis. The third study examined the test-retest reliability of cognitive tasks from the CANTAB testing instrument. These tasks were to be used in a protocol that required repeated assessments of cognitive performance separated by several hours in the same day. The aim of this study was to investigate the influence of practice and time of day effects

on the test-retest reliability of these tasks. The final study in this chapter examined the reliability of a computerised driving simulator scenario to assess driving performance. Driving simulators have distinct advantages to real-life driving, allowing tests to be conducted under conditions (i.e. alcohol intoxication) that would otherwise be too dangerous (Caird & Horrey, 2011; Creaser et al., 2011). This study was conducted to determine the test-retest reliability of performance measures collected during a repeated driving simulator scenario.

4.2 Pilot Study One - Development and Effectiveness of a Placebo Beverage Similar in Sensory Properties to an Alcoholic Beverage

Reader's Note:

The information in this section has been published as an original research paper:

Irwin C, Desbrow B, Leveritt M. Development and effectiveness of a placebo beverage similar in sensory properties to an alcoholic beverage. *Journal of Alcohol and Drug Education*, 2011; 55(3):p15-22.

The co-authors of this publication confirm that the research candidate has made the following contributions to this study:

- Developed the study design.

- Completed the human research ethics application.

- Designed and pilot tested the alcohol and placebo beverages.

- Conducted all participant recruitment and data collection.

- Conducted analysis of the data.

- Prepared manuscript for submission to journal.

- Presented research at a national conference.

Signed: _____   **Date: 06/09/13**

Signed: _____   **Date: 06/09/13**

4.2.1 Abstract

Aim: This pilot study was completed to develop an alcoholic and non-alcoholic (placebo) beverage that could not be distinguished from one another by taste or other sensory properties. **Methods:** Thirty-four volunteers participated in the study involving five tasting sessions (trials one to five) separated by at least one day each. Participants were randomly assigned to beverages for each trial and received a sample of liquid (~30ml) that was either an alcohol containing beverage (~12% v/v concentration) or placebo. An experimental tasting questionnaire containing six rating scales for the sensory properties of the drink was completed at each tasting session. **Results:** No difference in the proportion of participants' perceived alcohol concentration ratings was found between the groups for the first tasting trial. On subsequent trials (two to five), more participants were able to correctly identify the beverages. There was, however, no difference in the degree of uncertainty in participants' perception of the alcoholic content of the beverages in any of the trials. Mean ratings of sensory attributes were not different between the alcohol containing drink and placebo beverage in trial one. Higher ratings of acceptability were reported for the placebo beverage, and higher mean alcohol flavour intensity and alcohol burn/mouth-feel ratings for the alcohol containing drink were reported in trials two to five. No difference was observed between the two beverages for alcohol aroma intensity in any of the trials. **Conclusions:** These findings suggest that a placebo beverage prepared in accordance with the procedures used in this study has credibility in providing expectancy manipulation, particularly through olfactory cues. Additional methodological factors not used in this study, such as visual cues may improve the credibility of placebo deception.

4.2.2 Introduction

It is well established that alcohol consumption influences human behaviour and can cause impairment in cognitive function (Lane et al., 2004; Fillmore, 2007). However, evidence suggests that the behavioural and cognitive responses to alcohol may be mediated by the expectancy of alcohol consumption (Williams et al., 1981; Rohsenow, 1983; Hull & Bond, 1986; McMillen et al., 1989; Finnigan et al., 1995; Fillmore et al., 1998; Hammersley et al., 1998; Burian et al., 2003). The expectancy of receiving alcohol is dependent on factors that influence perception and can occur as the beverage is being consumed or sometime thereafter. Initially, individuals' expectations of alcohol consumption are influenced by their awareness of the beverage constituents and the sensory properties detected on consumption. In a research environment, awareness can be controlled by manipulating information provided to study participants. However, the sensory properties of the beverage are determined by the individual during consumption. Physiological effects are often delayed and are difficult to control. Generally, they are detectable when the dose of alcohol received elicits BACs of 0.08% or higher (Hammersley et al., 1992) and these effects usually confirm the initial expectancy of receiving alcohol.

Many studies employ a balanced placebo design, where a low- or non- alcoholic beverage serves as a control treatment, allowing for the effects of an alcohol intervention to be compared against a control. In order for the placebo arm of the intervention to be valid, it is important that participants are unable to detect the placebo beverage as a non-alcoholic drink, or at least have a high degree of uncertainty in their perception. Preparation of a non-alcoholic placebo beverage that imitates an alcoholic drink is challenging because of the distinct sensory attributes that are often associated with alcoholic drinks. Alcoholic beverages are often detected by subtle taste and olfactory cues, as well as other factors such as the mouth-feel of the beverage (Ross & Weller, 2008) and interoceptive intoxication cues that appear after ingestion (Williams et al., 1981).

In an effort to disguise placebo beverages, several studies have employed methods such as participants sucking on an anaesthetic throat lozenge prior to drink administration (Tiplady et al., 2004), mixing the drink with Tabasco sauce (Weissenborn & Duka, 2003; George et al., 2005) or peppermint flavouring (Tiplady et al., 2004; Tiplady et al., 2009), and preparing the placebo drink with a small amount of undiluted alcohol floated on the top, smeared around the rim of the glass, and/or sprayed as a mist over the drink (Lloyd & Rogers, 1997; Fillmore & Weafer, 2004; Fillmore et al., 2008; Ross & Weller, 2008). Typically, studies also have a significant time lapse between the repeated trials where tastings occur, reducing participants' ability to compare the different drinks. Validation of the placebo beverage occurs by asking participants to rate the alcoholic content of the beverages they receive within the study. Typically this is done by assessing the subjective effects reported by participants (Finnigan et al., 1995; Fillmore et al., 2008), comparing the beverage with standard alcoholic drinks (Fillmore et al., 1998; Fillmore & Vogel-Sprott, 2000; Fillmore, 2001; Fillmore & Blackburn, 2002; Fillmore & Weafer, 2004), or simply asking participants if they thought they had received an alcoholic drink (McMillen et al., 1989; Fillmore & Vogel-Sprott, 1998; Hammersley et al., 1998; Burian et al., 2003). These checks often reveal that the manipulation was successful and a credible placebo beverage was provided. However, participants

tend to report placebo beverages as having considerably lower alcohol content compared to the active dose conditions (Testa et al., 2006). Few studies actually report on participants' certainty of their perception.

The aim of this pilot study was to develop an alcoholic and non-alcoholic (placebo) beverage that could not be distinguished from one another by taste or other sensory properties. Participants' perceptions of the placebo beverage would then allow for an evaluation on the appropriateness of its use in a larger study examining the effects of dehydration and moderate alcohol consumption on cognitive function and reaction times.

4.2.3 Materials and Methods

Participants

Thirty-four volunteers (seven male and 27 female, mean age±SD = 24.7±6.2 yrs) participated in this study. Data related to personal alcohol drinking habits was not collected prior to participation in this study. However, no participant reported complete abstinence from alcohol. All participants were fully informed of the procedures of the study before giving their verbal consent. The investigation was approved by Griffith University's Human Research Ethics Committee (PBH/01/10/HREC).

Experimental Procedure

Each participant completed five trials separated by at least one day. On each day, participants were presented with a sample of liquid (~30ml) that was either an alcohol containing beverage or placebo. Participants were randomly assigned to beverages for each trial, so that half of the participants would receive an alcohol containing drink and half would receive a placebo drink for each trial. This design allows evaluation of drink order and its effect on participants' responses. The beverages were prepared outside of the participant's view and presented in white plastic cups

labelled only with the participants' initials. On administration of the beverage, participants were asked to first smell and then taste the drink by sipping the entire volume slowly. No time restraint was given for this process. At the same time, an experimental tasting questionnaire containing 6 rating scales and the following instructions were provided:

"You will be presented with a sample of liquid that either contains or does not contain alcohol, and asked to rate specific components of the beverage and your perception of the alcoholic concentration of the drink with certainty. Please taste the beverage and complete the following rating scales".

The questionnaire consisted of four sensory attribute statements. Participants were asked to rate the beverage for acceptability, alcohol aroma intensity, alcohol flavour intensity and alcohol burn/mouth-feel on an 11-point Likert scale (0 = dislike extremely, no alcohol; 10 = like extremely, extremely strong alcohol). Participants then rated their perceived alcohol concentration of the beverage (no alcohol, low alcohol, moderate alcohol, high alcohol) and their certainty of perception rating (not at all certain, somewhat certain, very certain, absolutely certain) using a 4-point Likert scale.

Beverages

The alcoholic drink (Fig. 4.2a) was formulated using vodka (Smirnoff®, 37% v/v ethanol) made up with equal parts of diet ginger beer cordial (Bundaberg Brewed Drinks Pty Ltd®) and diet ginger beer soft drink (Bundaberg Brewed Drinks Pty Ltd®), and one tenth the volume of diet lime cordial (Bickfords®, Australia). A large volume was made initially that contained 500ml vodka, 500ml ginger beer cordial, 500ml of ginger beer soft drink and 50ml of lime cordial, resulting in a beverage with an alcohol concentration of ~12% v/v which was stored in the refrigerator until

required, and decanted into ~30ml volumes for trial tastings. The placebo beverage (Fig. 4.2b) was identical to the alcoholic drink, however water was substituted for the vodka component. In addition, a mist of vodka was sprayed over the placebo beverage and on the rim of the plastic drink containers during the individual trial tastings to provide olfactory cues similar to that of the alcohol containing beverage.

Fig. 4.2a. Alcohol beverage ingredients.

Fig. 4.2b. Placebo beverage ingredients.

Statistical Analysis

All statistical procedures were performed using SPSS for Windows, Version 19.0 (SPSS Inc., Chicago, IL). Chi-square analysis was generated to compare the frequency distribution of ratings for the perceived alcohol concentration of the beverage and certainty of perception. Both scales were collapsed into three categories and analysis was conducted between groups (alcohol and placebo) for individual trials. Independent samples *t*-tests were conducted to reveal differences between the groups for each of the sensory attribute variables. Comparisons between trials for each group were conducted using one-way analysis of variance (ANOVA). Post-hoc analysis (LSD) was performed where significant main effects were present. All data are reported as mean±standard deviation unless otherwise specified. Statistical significance was accepted at $p<0.05$.

4.2.4 Results

Frequency distribution of ratings relating to the perception of alcohol concentration and certainty for each trial are shown in Fig. 4.2c. There was no difference in the proportion of perceived alcohol concentration ratings between the groups for trial one ($p>0.05$). On subsequent trials (two to five), there was a significant difference between the groups, with more participants able to correctly identify the beverages ($p<0.05$). However, there was a degree of uncertainty in participants' perception of the alcoholic content of the beverages, with high ratings of 'somewhat certain' in many of the trials. No differences in certainty were found between the two groups in any of the trials ($p>0.05$).
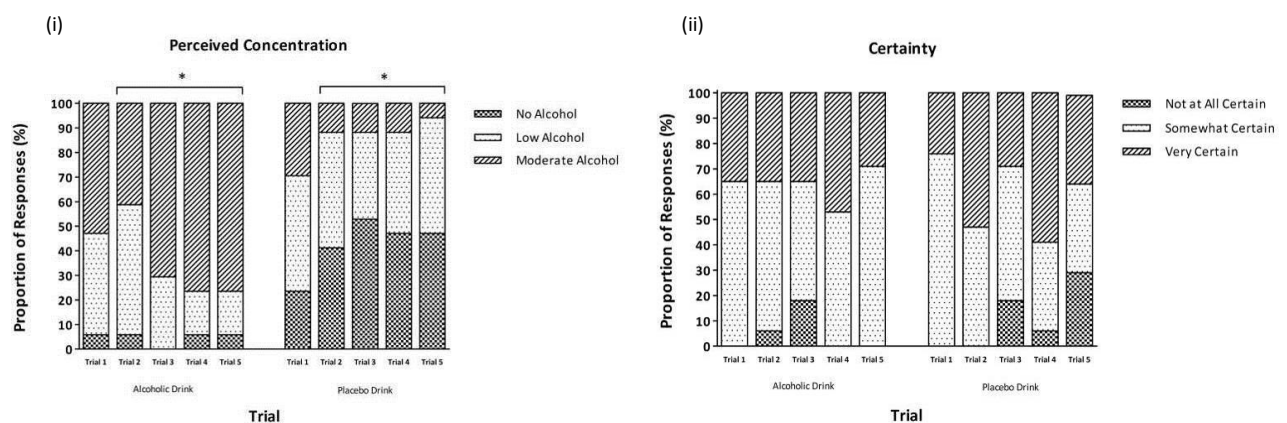
Fig. 4.2c. Subjective ratings: (i) Perceived alcohol concentration; (ii) Certainty of perception. * Significant difference between groups.

Mean ratings of sensory attributes for each trial are shown in Fig. 4.2d (i-iv). Participants reported no difference in any of the sensory attributes between the alcohol containing drink and placebo beverage in trial one ($p>0.05$). On all subsequent trials there was a significant difference between the two beverages with higher mean acceptability ratings reported for the placebo beverage, and higher mean alcohol flavour intensity and alcohol burn/mouth-feel ratings for the alcohol containing drink ($p<0.05$). No difference was observed between the two beverages for alcohol aroma intensity in any of the trials ($p>0.05$).

Acceptability of Beverage

Alcohol Flavour Intensity

Alcohol Burn/Mouth Feel
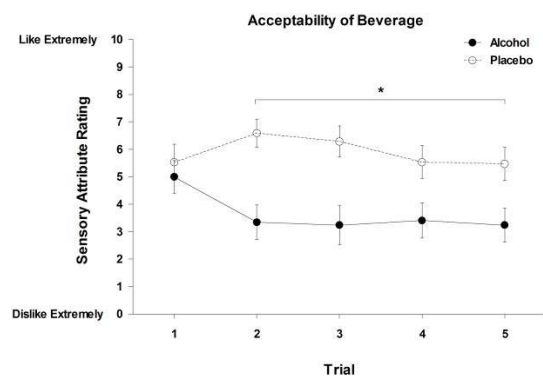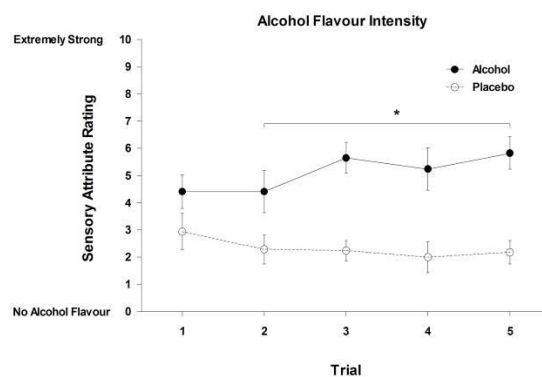
Alcohol Aroma Intensity
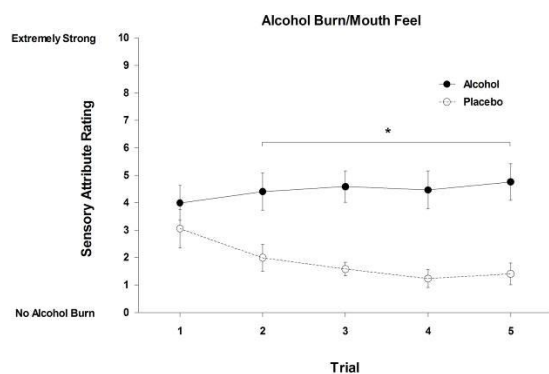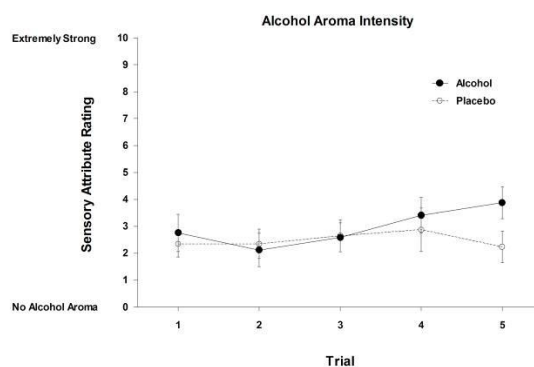
Fig. 4.2d. Subjective ratings of sensory attributes: (i) Acceptibility of the beverage; (ii) Alcohol aroma intensity; (iii) Alcohol flavour intensity; (iv) Alcohol burn/mouth-feel. * Significant difference between alcohol and placebo beverage ratings. Values are mean±SEM.

4.2.5 Discussion

The aim of this pilot study was to develop an alcoholic and non-alcoholic (placebo) beverage that could not be distinguished from one another by taste or other sensory properties. Results from this study show that a placebo beverage prepared in accordance with the procedures outlined in the methods has credibility in providing expectancy manipulation.

The ginger beer ingredients used in the preparation of the beverages may have provided some sensory cues similar to an alcoholic drink, which is indicated by no difference in the ratings of alcohol flavour intensity and alcohol burn/mouth-feel between the two beverages in the first taste testing trial. Participants possessed a greater ability to identify the placebo beverage in subsequent trials, which suggests that the cues received from the first trial allowed comparison of

the drinks and greater detection of differences between beverages. However, the degree of certainty did not change throughout, with most participants only 'somewhat certain' of their perception. This suggests that there may have been some degree of guessing by participants when selecting the perceived alcohol concentration rating of the beverage and provides some evidence for successful manipulation of the non-alcoholic drink.

Based on the alcohol aroma intensity alone, participants were not able to distinguish between the alcohol and placebo beverages throughout trials. The alcohol mist sprayed over the placebo was successful in providing olfactory cues that imitated the ethanol aroma in the alcohol containing drink. Whilst other cues such as the flavour and mouth-feel were rated different between the beverages, similar ratings of alcohol aroma intensity between the drinks suggest that the aroma of the beverage may have provided the cue to instigate a degree of uncertainty in participants' perception of alcohol concentration.

Several studies have employed methods where beverages are prepared in front of the participant (Finnigan et al., 1995; Burian et al., 2003). In these cases, commercial alcohol containers are filled with water and standard measures are used to prepare the placebo drink, allowing participants a visual perception of alcohol preparation when in fact they are receiving placebo. The preparation of placebo beverages allowing visual cues has been suggested to have the strongest association with placebo credibility (Rohsenow & Marlatt, 1981). Viewing the preparation of beverages did not occur in the present study. In addition, participants were told that they may receive either an alcoholic or placebo beverage at each trial. An awareness of the placebo beverage may influence participants' expectancy of alcohol and result in an overestimated detection rate of the placebo. Slight procedural manipulations such as preparing the drinks in front of the participant and giving an expectancy of receiving only an alcoholic beverage may have induced different results, particularly in subjective ratings of perceived concentration and

certainty of perception throughout the trials. These additional procedural factors are recommended for administration of the beverages in the main study.

In summary, this study examined the effectiveness of a non-alcoholic beverage as a placebo compared to an alcoholic drink with similar sensory properties. A placebo beverage prepared in accordance with the procedures outlined in the methods of this study has credibility in providing expectancy manipulation, particularly through olfactory cues. However, additional factors that were not used in this study, such as visual cues through the preparation of beverages in front of participants may improve the credibility of the deception and should be explored when undertaking future studies. The placebo beverage designed and tested in this study will be implemented in Research Studies Three (Chapter Seven) and Four (Chapter Eight) to examine the expectancy effects of alcohol on measures of cognitive and simulated driving performance.

4.3 Pilot Study Two - Accuracy and Reliability of Breath Alcohol Analysis Following Exercise-Induced Dehydration

4.3.1 Abstract

Aim: This study investigated the influence of hydration status on the accuracy and reliability of alcohol concentrations determined by breath analysis. **Methods:** Twelve male volunteers participated in three experimental trials completed in a randomised cross over design and separated by at least seven days each. In one trial, participants exercised to cause dehydration of ~2.5% body weight loss. For the other trials participants were required to be in a rested and euhydrated state. A set volume of alcohol was then consumed in each trial and participants were monitored over a four hour period. Blood (BAC) and breath (BrAC) alcohol samples were collected throughout and analysed to determine the quantitative relationship between the two methods of analysis. **Results:** Blood and breath alcohol concentrations showed a good correlation, with no difference between relationships for the dehydration ($r = 0.76$) and euhydration trials ($r = 0.83$). The breathalyser showed a proportional and constant bias under each of the trial conditions, with estimates tending to read too high in comparison to coexisting concentrations of alcohol determined from venous blood specimens. **Conclusions:** Dehydration producing a 2.5% loss in body weight appears to have no influence on the accuracy and reliability of breath alcohol analysis. However, the results from this study suggest that breath alcohol concentrations may overestimate concentrations in the venous blood, disadvantaging a motorist being tested at the roadside.

4.3.2 Introduction

Driving a motor vehicle whilst under the influence of alcohol continues to be an important public health concern in Australia. The consumption of alcohol increases the risk of motorists being involved in an accident that could have fatal consequences (Blomberg et al., 2005). It is estimated that ~30% of all driver and pedestrian fatalities on Australian roads are alcohol related (Chikritzhs et al., 2000). In an attempt to lower road fatality rates, statutory alcohol limits are enforced as a means of reducing alcohol-impaired driving. Australia, like many other countries imposes a BAC limit of 0.05% for individuals operating a motor vehicle. Despite the consequences associated with drink driving and the prospect of being randomly tested for alcohol intoxication on any Australian road, many people still risk their lives and the lives of others by driving with concentrations of alcohol in their blood that impair their road use skills (World Health Organisation, 2007).

The medico-legal diagnosis of alcohol intoxication is typically achieved through the analysis of venous blood samples, a method often considered as the 'gold standard' (Haggard et al., 1940). However, blood sampling techniques are impractical at the roadside and breath alcohol measuring

instruments (breathalysers) have been designed to provide law enforcement officers with an efficient and practical means of measuring the BAC of motorists in the field. Some concerns have emerged over the accuracy and precision of breathalysers with many physiological and analytical variables affecting the reliability of breathalyser readings (Rose & Furton, 2004).

One biological factor that may influence the reliability of these devices is the hydration status of the individual being tested. The distribution of alcohol to various compartments of the body is largely governed by the water content of the respective tissues and organs (Eckardt et al., 1998). A reduction in total body water content caused by exercise induced fluid loss is expected to decrease water volume in the tissues, reducing the dilution of alcohol in these compartments (Pohorecky & Brick, 1988). This could consequently affect the accuracy and precision of the breathalyser when samples are collected under these conditions. Accuracy and precision considerations become very important where BrAC levels are close to the statutory alcohol limits as results from breath analysis can be used to legally classify intoxication and a criminal conviction recorded for driving under the influence of alcohol when a BAC reading is measured at or above 0.05%.

The Alcolizer Law Enforcement (LE) testing device has been designed and developed with the support and input from Australian and international law enforcement agencies. According to the manufacturer's product statement (Alcolizer Technology, www.alcolizer.com), this device offers advanced technology screening and evidential standard accuracy within ±5%. However, there are no published studies examining the effect of hydration status on the reliability of breath alcohol analysis. In this investigation the accuracy and reliability of breath alcohol analysis measured by the Alcolizer LE instrument was determined under different conditions of hydration status (dehydrated and euhydrated). Concentrations of alcohol in venous blood were compared to measures calculated from end expired breath for each of the hydration conditions. The quantitative relationship between BAC and BrAC was evaluated by two different statistical

91

methods; correlation-regression analysis (Bland & Altman, 1986a; Leatherbarrow, 1990; Altman, 1991) and the method of differences proposed by Bland and Altman (Altman & Bland, 1983; Bland & Altman, 1986b, 1999).

4.3.3 Materials and Methods

Participants

Twelve healthy Caucasian males (22.6±4.2 yrs, 77.2±6.9 kg BW, 180.5±5.0 cm; values are mean±SD) volunteered to participate in this study. Participants had a history of alcohol consumption of 5.8±4.4 years. The self-reported intake of alcoholic beverages was equivalent to 5.9±2.3 standard drinks (based on the consumption of alcohol from a range of sources including beer, wine and spirits that contain 10g of ethanol) and drinking frequency was reported as 1.0±0.8 times per week using the personal drinking history questionnaire (Vogel-Sprott, 1992). All participants were fully informed of the nature and possible risks of the study before giving their written informed consent. The investigation was approved by Griffith University's Human Research Ethics Committee (PBH/01/10/HREC).

Experimental Design

Each participant completed three experimental trials using a randomised and counterbalanced design, with each trial separated by at least seven days. Trials were conducted at the same time of the day in a stable laboratory environment (22±2°C, 60-70% RH). In one trial, participants were required to perform exercise to cause dehydration through sweat loss for an approximate BW loss of 2.5% (Fig. 4.3a, i). This level of fluid loss equates to approximately 1.8kg (equivalent to ~1.8 litres of sweat) in a 70kg person, and is not unusual in sporting participants and individuals employed to do manual labour (Sharp, 2006; Kenefick & Sawka, 2007; Maughan, Watson, et al.,

2007; Benelam & Wyness, 2010). For the other two trials, participants were not required to complete the exercise component (Fig. 4.3a, ii).
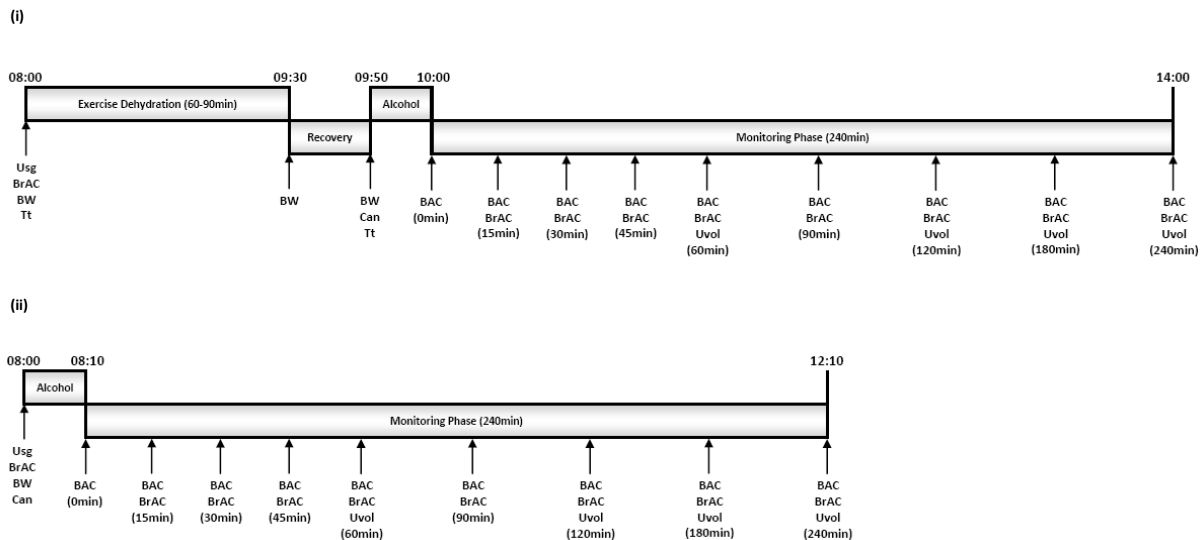
Fig. 4.3a. (i) Experimental trial procedure for the dehydration and alcohol trial (DA); (ii) Experimental trial procedure for the euhydration and alcohol trials (A1 & A2). U_{sg}, Urine specific gravity measure; BrAC, Breath alcohol concentration measure; BAC, Blood alcohol concentration measure; BW, Body weight measure; Can, Cannulation; Tt, Tympanic temperature measure; Uvol, Urine volume measure.

Pre-Experimental Procedures

Participants were asked to abstain from alcohol for 24hrs, and caffeine-containing substances and moderate-strenuous exercise for 12hrs, prior to each experimental trial. In addition, participants were asked to fast from all food and beverages (except water) for 12hrs prior to each trial. Participants were instructed to drink plenty of fluid on the day preceding each experimental trial to assist with hydration and to consume at least 500ml of water before going to bed. During the 24hr period immediately preceding the first trial, participants recorded all food and beverages consumed as well as any exercise completed. A food and exercise record was supplied to each participant and they were asked to repeat this on the day prior to all subsequent trials.

Experimental procedures

Participants arrived at the laboratory in a fasted condition at approximately 08:00hrs. Compliance with pre-experimental conditions was confirmed verbally on arrival before a urine sample was collected to calculate U_{sg} as an initial measure of hydration status (Digital Urine Specific Gravity Refractometer UG-α (alpha)®, ATAGO Co. Ltd, Tokyo, Japan). Participants who recorded a U_{sg} reading >1.020, indicating some level of pre-existing hypo-hydration (Sawka et al., 2007), were provided with additional water until a urinary sample fell below the accepted threshold. Only two participants required water (840-1200ml) on one trial each, which was consumed over 60 min. Measures of BrAC were then taken to confirm abstinence before proceeding with the trial.

During one of the trials, participants were required to exercise to cause dehydration (trial DA). For this trial, participants voided their bladder completely after the initial BrAC measure and an initial nude body weight was then measured. After the body weight, dehydration was induced by continuous exercise on a cycle ergometer (Monark, Ergomedic 828E, Vansbro, Sweden) at an intensity corresponding to ~70-80% of maximum heart rate (HR_{max}). During the exercise ride, participants wore warm clothing including tracksuit pants and a long sleeve jumper to assist with sweat loss (Fig. 4.3b). The intention was to induce dehydration equivalent to 2.5% BW loss. Participants would stop exercise once they had reached ~2.3% BW loss, with the remaining loss expected to occur during the subsequent resting period.

Fig. 4.3b. Dehydration cycling protocol.

At the end of exercise, participants took a cool shower before drying themselves thoroughly and measuring a final nude body weight. Estimations of TBW content and loss were then calculated from the change in BW using the equation proposed by Watson et al. (1980). Participants then rested in a supine position while a 21-gauge venous cannula was inserted into a superficial forearm vein to allow subsequent collection of blood samples for the analysis of BAC.

In the other two trials, exercise was not performed (trial A1 and A2) and following the initial BrAC measure, participants voided their bladder completely before the venous cannula was inserted to enable blood sample collection. Following cannulation in all three trials, participants were provided with a set volume of alcohol administered as vodka (Smirnoff®, 37% v/v ethanol) made up with orange juice (Just Juice®, National Foods, Australia) in a ratio of one part vodka to two parts orange juice. For the first experimental trial the volume of the alcoholic beverage was individually calculated with the intention of raising BAC to ~0.050% (Watson, et al., 1981). In the subsequent trials, the same volume of alcohol was used as previously calculated. Participants were asked to consume each drink at a steady pace over 10 min. Immediately following consumption, a 5ml venous blood sample was collected from the cannula site for subsequent analysis of BAC.

Participants then rested in a seated position in the laboratory, whilst being monitored over a four hour period. No fluid or food was consumed throughout the monitoring period. Blood and breath alcohol samples were collected every 15 min for the first hour, every 30 min for the second hour and every hour thereafter for a total of four hours. Participants were asked to void any urine at each hour of the monitoring phase, which was collected in containers and subsequently weighed to calculate cumulative urine loss. At the end of the trial, participants were provided with snacks and drinks, and given taxi vouchers to ensure safe transportation home.

Breath alcohol concentrations

Breath alcohol concentrations were analysed using a police grade Alcolizer LE breathalyser (Alcolizer Pty Ltd, Brisbane, QLD, Australia), which had been recently calibrated by the manufacturer (Fig. 4.3c). All breathalyser measurements were taken in duplicate, with a triplicate measure recorded if readings differed by ≥0.005%. The measures were averaged to provide the final assessment of BrAC. Participants were not informed of their BrAC measures until after completion of the entire study.

Fig. 4.3c. Alcolizer hand-held breathalyser.

Assay of ethanol and pharmacokinetic analysis

Samples of venous blood were obtained from a cannula that had been inserted into a superficial forearm vein at 0, 15, 30, 45, 60, 90, 120, 180 and 240 min time intervals following the ingestion of the alcoholic beverage. The 5ml blood samples were collected into vacutainer tubes containing 30 mg sodium fluoride and centrifuged at 3000 rpm for 10 min. The resultant plasma was stored at -84°C for subsequent analysis of ethanol. The concentrations of ethanol were determined in the plasma samples using the Ethanol Gen.2 enzymatic method on a COBAS Integra 400 auto-analyser (Roche Diagnostics®, Mannheim, Germany). Plasma samples were prepared with reagents and the assays compared to commercially available standards in accordance with the manufacturer's specifications. Plasma concentrations were converted to equivalent whole

blood concentrations using an average ratio between plasma and whole blood of 1.14:1 (Winek & Carfagna, 1987; Charlebois et al., 1996). The procedure for these calculations has been outlined previously (Harding, 2003).

Statistical Analysis

All statistical procedures were performed using SPSS for Windows, Version 19.0 (SPSS Inc., Chicago, IL). Linear regression analysis was performed on the duplicate breath alcohol measurements under the two hydration conditions (Bland & Altman, 1986a; Leatherbarrow, 1990; Altman, 1991). This procedure was also used to compare blood and breath alcohol concentrations, with BrAC chosen as the independent variable (*x-variate*) and BAC as the dependent variable (*y-variate*). The slope and intercept of the regression line indicates the presence of proportional and constant bias between BAC and BrAC respectively, and random variation is given by the residual standard deviation (*r*SD) (Westgard & Hunt, 1973; Ludbrook, 1997). For this analysis, data from the two euhydration and alcohol trials (A1 and A2) were combined. Bland and Altman's method was also used to calculate bias and imprecision between blood- and breath-alcohol analyses (Altman & Bland, 1983; Bland & Altman, 1986b, 1999). The mean and standard deviation (SD) of the individual BAC - BrAC differences are indicators of bias (accuracy) and random variations, respectively. The mean and SD of the differences were then used to calculate the 95% limits of agreement (LOA) and the associated confidence limits.

4.3.4 Results

Duplicate breath-alcohol measurements

Scatter plots for the euhydration and alcohol trials (A1 & A2), and dehydration and alcohol trials (DA) are shown in Fig. 4.3d and Fig. 4.3e respectively. A high correlation is indicated for both hydration conditions ($r = 0.99$, $p<0.01$). Regression equations were identical under both trial

conditions (BrAC2 = 0.99BrAC1 + 0.000) and the low residual SD of 0.002% indicates almost perfect 1:1 agreement. About 95% of differences between duplicate measures of BrAC were within ±0.004% (1.96 x 0.002).

Fig. 4.3d. Association between duplicate breath-alcohol measurements for the euhydration and alcohol trials (A1 & A2), where n is number of x–y pairs, r is the correlation coefficient and rSD is the residual standard deviation or random error, dotted lines represent 95% prediction intervals. The regression equation was BrAC2 =0.995 BrAC1 + 0.000.

Fig. 4.3e. Association between duplicate breath-alcohol measurements for the dehydration and alcohol trials (DA), where n is number of x–y pairs, r is the correlation coefficient and rSD is the residual standard deviation or random error, dotted lines represent 95% prediction intervals. The regression equation was BrAC2 =0.999 BrAC1 +0.000.

Regression of blood- on breath-alcohol concentration

Scatter plots for the euhydration and alcohol trials (A1 & A2), and dehydration and alcohol trials (DA) are shown in Fig. 4.3f and Fig. 4.3g respectively. The correlation coefficient calculated for the euhydration and alcohol trials was r = 0.83 ($p<0.01$), with 68% (r^2) of the variance in BAC explained by the linear regression on BrAC. The slope of the regression line was 0.535 ± 0.027 (ideally this should be equal to unity) indicating that concentrations determined by the breathalyser read low by ~46% on average. The y-intercept was 0.012 ± 0.001% (ideally this should be equal to zero) indicating a constant bias and verifying that when the breathalyser indicates a value of 0.000%, measurable amounts of alcohol are still likely to be present in venous blood. From the regression equation for these trials it can be shown that for a mean BrAC of 0.050%, the expected venous BAC will be ~0.039%. Similar results were found for the dehydration and alcohol trial conditions.
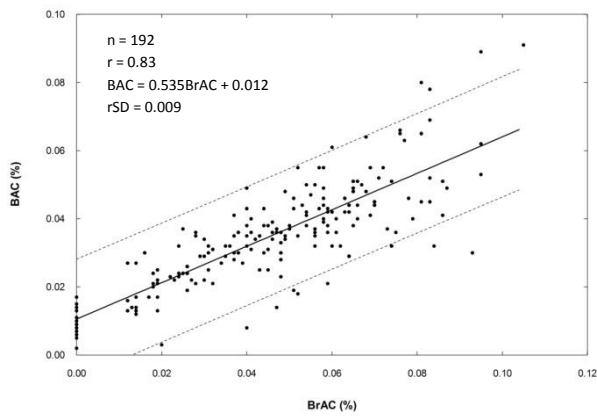
Fig. 4.3f. Scatter plot of venous blood-alcohol (y-variate %) and breath-alcohol (x-variate %) for euhydration and alcohol trials (A1 & A2), where n is number of x-y pairs, *r* is the correlation coefficient, *r*SD is the residual standard deviation or random error, dotted lines represent 95% prediction intervals.
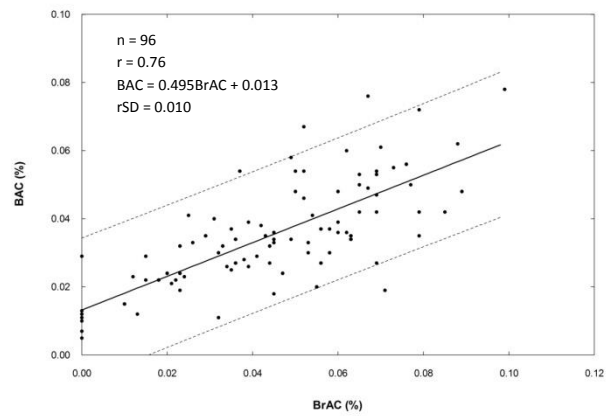
Fig. 4.3g. Scatter plot of venous blood-alcohol (y-variate %) and breath-alcohol (x-variate %) for dehydration and alcohol trials (DA), where n is number of x-y pairs, r is the correlation coefficient, rSD is the residual standard deviation or random error, dotted lines represent 95% prediction intervals.

Differences between blood- and breath-alcohol concentrations

A separate Bland-Altman plot was developed for the euhydration and alcohol trials (A1 & A2; Fig. 4.3h) and the dehydration and alcohol trials (DA; Fig. 4.3k). In each plot, the difference in measures between analytical methods (BAC - BrAC) was plotted against the mean concentration of alcohol (BAC + BrAC)/2. For the euhydration and alcohol trials (A1 & A2), the observed bias was -0.012% and the standard deviation of differences was 0.014%, so that the 95% limits of agreement for results by the two analysis methods were -0.039% and 0.018%. Consequently, when the breathalyser is used to estimate venous blood alcohol concentration under conditions where individuals are in a euhydrated and rested state, the results will tend to be too high with a mean bias of 0.012% and 95% of values being between 0.018% low and 0.039% high. Similar results were also found for the dehydration and alcohol trial conditions using this method.
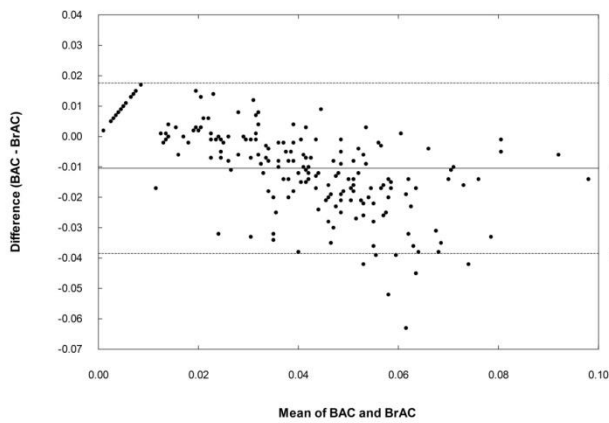
Fig. 4.3h. Bland-Altman plot of individual differences (BAC - BrAC) against the average of the two measurements (BAC + BrAC)/2 for the euhydration and alcohol trials (A1 & A2). The horizontal dotted lines show mean bias -0.012 and 95% limits of agreement (LOA) -0.039 and 0.018.
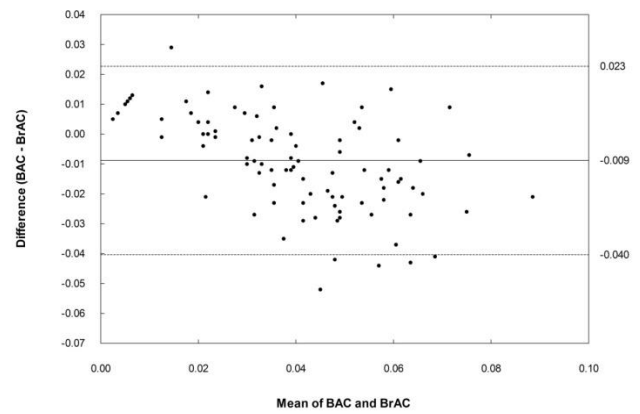
Fig. 4.3k. Bland-Altman plot of individual differences (BAC - BrAC) against the average of the two measurements (BAC + BrAC)/2, for the dehydration and alcohol trials (DA). The horizontal dotted lines show mean bias -0.009 and 95% limits of agreement (LOA) -0.040 and 0.023.

4.3.5 Discussion

This study examined the influence of hydration status on the accuracy and reliability of alcohol concentrations determined by the Alcolizer LE breath analyser. Results from the breathalyser were compared to alcohol concentrations determined in venous blood samples collected concurrently with breath analysis. A comparison of breath with blood analysis indicates a relatively high accuracy of the Alcolizer LE device, with no effect of hydration status on the reliability of the readings. The value of correlation coefficients for the relationship between the readings of the breathalyser and blood analysis were comparable under both hydration conditions in this study. Contrary to some beliefs that dehydration may influence the partition ratio between blood and breath alcohol concentrations and in turn affect the reliability of breath analysis (Thompson, 1997), the results from this study suggest that readings from the Alcolizer LE breathalyser are not affected by dehydration producing a 2.5% loss in body weight.

Random variation between BAC and BrAC, indicated by residual standard deviations of 0.010% (DA trial) and 0.009% (A1 and A2 trials) were in close agreement with the standard deviation of differences (BAC – BrAC) of 0.016% and 0.014% for the DA trial and A1 + A2 trials respectively. The Bland-Altman plots indicated that readings from the breathalyser slightly overestimated alcohol concentrations in comparison to blood specimens, with hydration status having no effect on these

differences. Some measures in each of the hydration conditions appeared to be outliers, reducing the overall accuracy of the breathalyser results compared to the blood results. However, it is important to note that BrAC measurements were collected at 15 min intervals immediately following alcohol consumption, whilst in the alcohol absorption phase. At this time, equilibrium between the blood and breath tissues is not yet established (Zuba, 2008) and concentrations of alcohol in breath more closely reflect concentrations in arterial blood rather than venous blood (Martin et al., 1984; Jones & Andersson, 2003). In this study venous blood specimens were analysed, which may explain the existing outliers observed in some measurement comparisons.

No studies have specifically investigated the accuracy and reliability of the breathalyser model used in this investigation. However, several studies have examined the accuracy and reliability of many other available devices (Martin et al., 1984; Jones & Andersson, 2003; Lindberg et al., 2007; Zuba, 2008; Peleg et al., 2010). Jones & Andersson (2003) observed a high correlation (r=0.97) between measures taken by breath analysis using the Intoxilyzer 5000S and venous blood samples. Participants were provided with 0.40-0.65 g/kg body weight of alcohol and had BAC and BrAC measures collected at 30 min intervals from one hour post ingestion. Contrary to the current study, the authors found that the breathalyser almost always underestimated BAC, resulting in lower BrAC results compared to the blood specimens and favouring the subject being tested. Martin et al. (1984) also observed highly accurate and reproducible results with the Alcolinger automatic breath analyser in subjects which provided different doses of alcohol (0.5g/kg, 0.75g/kg, 1.0g/kg, 1.25g/kg body weight). However, the authors noted that different breath alcohol profiles were observed compared to venous blood alcohol profiles, which was most pronounced in subjects given the low dose of alcohol (0.5g/kg body weight). At this dose BrAC overestimated the BAC from venous blood, particularly during the absorption phase (60-120 min post ingestion), and more closely resembled measures taken from arterial blood which led the authors to conclude that BrAC is more closely correlated with arterial BAC during alcohol

101

absorption. A recent study by Lindberg et al. (2007) supports this statement with the authors finding that BrAC measured on a prototype breath analyser closely reflected arterial BAC, but not venous BAC. There are some indications that complete post-absorptive status may not actually occur until more than three hours after drinking and as a consequence, breath test results may tend to overestimate actual BAC for significant amounts of time after peak BAC has been reached (Simpson, 1989).

Handheld breathalyser devices are usually used at the roadside for the initial testing of alcohol intoxication in motorists (Zuba, 2008). Evidence suggests that the majority of drinking drivers are in the post-absorptive phase of alcohol kinetics when they are tested (Jones & Andersson, 1996). Thus, although results from breathalyser analysis may not provide direct correlation of venous BAC in the absorption phase, most drivers are tested when a better relationship between the two measures does exist. According to the Transport Operations (Road Use Management) Act 1995 (Office of the Queensland Parliamentary Counsel, 2011) the statutory alcohol limit in Australia is defined as a concentration of alcohol in a person's blood equal to or more than 50mg of alcohol in 100mL of blood; or the concentration of alcohol in a person's breath equal to or more than 0.050g of alcohol in 210L of breath. A person caught operating a motor vehicle with alcohol in their system at or above these levels can be lawfully detained and charged for driving under the influence (DUI). Based on these classifications, one would expect breath alcohol devices to accurately reflect the concentration of alcohol in the blood at all times, particularly since initial measures of intoxication are calculated with handheld breathalysers.

The Alcolizer LE device is designed and calibrated to provide readings reflecting the number of grams of alcohol per 210L of breath. Thus the readings provided from a breath specimen should be equivalent to measures analysed in blood samples. Results from this investigation indicate that the Alcolizer breathalyser device has a tendency to give higher readings compared with venous BAC measures. However, this likely reflects bias achieved through analysis of BrAC during the

absorption phase of alcohol, as measures were taken from 15 min post ingestion. Motorists tested for alcohol intoxication on the Alcolizer device are likely to be disadvantaged during the absorption phase in comparison to venous blood samples. Although previous research has also indicated that breath test results may also overestimate actual BAC for significant amounts of time after peak BAC has been achieved (Simpson, 1989).

In summary, the results of this investigation indicate a good correlation between the readings of the Alcolizer LE breathalyser and blood analysis. In addition, it appears that hydration status has no impact on the reliability of the breathalyser results. Whilst breath analysis measures taken during the absorptive phase of alcohol may provide higher readings than venous blood samples, this may be beneficial in the field, allowing police officers to detain motorists with high initial readings for subsequent analysis and verification in the post-absorptive state prior to recording a DUI conviction. The breathalyser employed in this study will be used in Research Studies Two (Chapter Six), Three (Chapter Seven) and Four (Chapter Eight) to provide measures of intoxication level following alcohol consumption under various levels of hydration status.

4.4 Pilot Study Three - Test-Retest Reliability of CANTAB Neuropsychological Tasks: Effects of Practice and Time of Day with Brief Test-Retest Intervals

4.4.1 Abstract

Aim: This study investigated the influence of practice and time of day effects on the test-retest reliability of four tasks (viz. Choice Reaction Time, Match to Sample visual search, Stop Signal Task, Stockings of Cambridge) from the CANTAB cognitive test battery. **Methods:** Ten volunteers (four male, six female) completed two cognitive assessments, one in the morning and one in the afternoon on the same day, separated by approximately five hours. **Results:** Mean correct reaction time on the MTS Task was faster in the repeated test compared to the initial assessment, indicating a significant effect of practice. No practice effects were observed for any of the other measured variables in any of the cognitive tasks. Test-retest reliabilities were excellent and within or above ideal values ($r = 0.75\text{-}0.8$) for the CRT and SST tasks. Reliability coefficients were below ideal values for most measures from the MTS and SOC tasks indicating only modest test-retest reliability. **Conclusions:** Results from this study suggest that some tasks from the CANTAB battery may not meet the proposed ideal level of test-retest reliability for use in repeated assessments of cognitive performance. Some caution should be exercised before generalising these findings due to the low sample size employed in the study. However, the results do reinforce the importance of measuring test-retest reliability of cognitive tasks that are proposed for use in future studies.

4.4.2 Introduction

Cognitive testing is the process of determining an individual's cognitive strengths and weaknesses using qualitative (approach to tasks and observed behaviour) and quantitative (standardised and scaled measurements) approaches (Galotti, 2013). Historically, cognitive testing has been accomplished through the use of pencil and paper tasks to assess a wide range of abilities, including attention, memory, problem-solving and intellectual functioning. An assessment using these tools would typically take a few hours to administer, score and interpret for each individual (Dwolatzky et al., 2003). Fortunately many of the traditional pencil and paper tests have now been incorporated into computerised cognitive testing batteries, which claim to offer assessment instruments that are practical, simple to use, have relatively small testing times, use an objective and automatic scoring process, have been extensively validated, and have high test-retest reliability (Collie & Maruff, 2003).

Computerised neuropsychological tasks have been used to increase our understanding of deficits in cognitive functioning that are thought to occur with ageing (Robbins et al., 1994; Fray &

Robbins, 1996; Robbins et al., 1998), and in populations diagnosed with clinical disorders such as Alzheimer's disease (Egerhazi et al., 2007) and Schizophrenia (Stip et al., 2008). Researchers have also used these instruments to assess cognitive function in response to pharmacological challenges (Durlach, 1998; Weissenborn & Duka, 2003; Makela et al., 2005). These studies typically involve the repeated administration of tasks before and after a treatment protocol, and their validity depends on the assumption that the tests employed have high test-retest reliability (Lowe & Rabbitt, 1998). There are implications for the use of assessment tasks that have low test-retest reliability in clinical settings, as they are limited in the extent to which the tests can be expected to correlate with other measures and also in the test's sensitivity to detect changes in performance when administered repeatedly (Lowe & Rabbitt, 1998). An additional problem with repeated testing is that improvement with practice may occur; known as the practice effect (Beglinger et al., 2005). This is normally most pronounced when intervals between testing are short and could potentially mask other effects that may be present, leading to confounding results (Collie et al., 2003). In situations where serial testing is performed across several hours of a single day, it is also important to consider time of day effects that may influence assessment outcomes. Neurobehavioural factors are subject to circadian rhythmicity, modulated hour-to-hour over a wake cycle and can be reflected by changes in fatigue, alertness, and performance (Van Dongen & Dinges, 2000).

The Cambridge Neuropsychological Test Battery (CANTAB) is a computerised neuropsychological assessment instrument that contains 22 computerised tasks. These are broadly classified into six main areas of cognitive function including general memory and learning; visual memory; planning, working memory and executive function; attention and reaction time; semantic/verbal memory; and decision making and response control (Cambridge Cognition Limited, 2006). Many studies support the validity and use of neuropsychological assessment by the CANTAB (Lange et al., 1992; Robbins et al., 1994; Fray & Robbins, 1996; Fowler et al., 1997;

Robbins et al., 1998; Louis et al., 1999; Weissenborn & Duka, 2003; Egerhazi et al., 2007). However, little is known about the test-retest reliability of many of the tasks included in the CANTAB program. Lowe & Rabbitt (1998) measured the test-retest reliability for three of the CANTAB cognitive domains (viz. visual memory, working memory and planning, attention) in a large group (n=162) of healthy elderly (60-80 yrs) volunteers. The authors administered the tests on two occasions separated by an interval of four weeks and found that tests varied markedly in test-retest reliability. In several cases test-retest correlations fell below 0.75; the level considered methodologically acceptable (Coolican, 2004), and some tests showed significant practice effects that were considered substantial enough to compromise comparisons on repeated testing. Results from this study suggest that the robustness of test-retest reliability of neuropsychological tasks on the CANTAB cannot be taken for granted and must be documented whenever they are used (Lowe & Rabbitt, 1998).

Studies that incorporate neuropsychological tests into a design examining the effects of pharmacological treatments (e.g. alcohol, caffeine) often administer repeated tests with much shorter delays than those typically observed in clinical interventions, and in a younger population group (Hindmarch et al., 1991; Durlach, 1998). Given that practice and time of day effects are likely to be more pronounced with shorter re-test intervals, there is greater potential for the reliability of these testing instruments to be affected in these studies. However, few studies have examined the test-retest reliability of neuropsychological assessment instruments administered at brief retest intervals (Collie et al., 2003) and there appears to be no literature examining test-retest reliability of CANTAB tasks at short test-retest intervals.

The purpose of this study was therefore to determine the test-retest reliability of four tasks from the CANTAB (viz. Choice Reaction Time, Match to Sample-visual search, Stop Signal Task, Stockings of Cambridge) to examine the effects of practice and time of day on cognitive performance variables.

4.4.3 Materials and Methods

Participants

Ten healthy volunteers (four male, six female) whose ages ranged from 19 to 36 yrs (mean±SD = 26.0±7.5 yrs) participated in this study. At the time of testing, participants were either current students or staff members at Griffith University. Participants were asked to refrain from consuming alcohol and caffeine containing products on the day of testing until all of the tests were complete. Compliance to the study requirements was verbally acknowledged prior to the administration of tests. The investigation was approved by Griffith University's Human Research Ethics Committee (PBH/01/10/HREC).

Experimental Procedures

Assessment of cognitive performance was completed using a four task CANTAB protocol. The tests were administered using an IBM personal computer with a touch sensitive screen (Fig. 4.4). Participants completed the test battery on two occasions on the same day and were seated in a quiet room. The first test was completed in the morning between 09:00 and 12:00hrs (Test 1). Participants returned to complete a retest of the CANTAB battery in the afternoon between 14:00 and 17:00hrs (Test 2). The tests were administered in accordance with the instruction manual for each task.
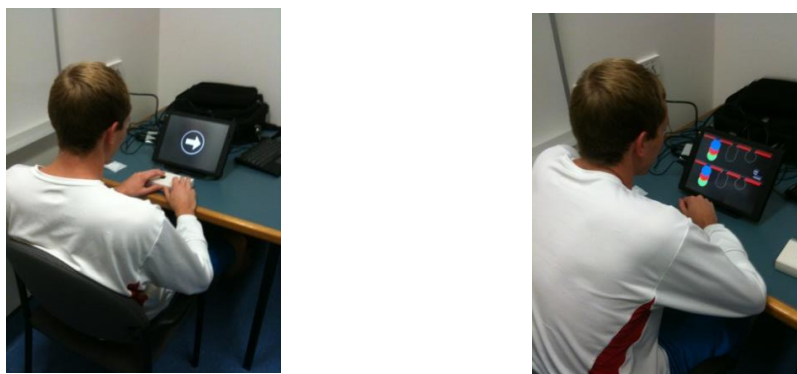
Fig. 4.4. CANTAB testing instrument.

Cognitive Test Battery (CANTAB)

The four tasks administered on the CANTAB test battery were completed in the order as listed (the technical description of the tests can be found on the Cambridge Cognition website: http://www.cantab.com): Choice Reaction Time (CRT): This task measures speed of response in a simple two choice protocol with outcome measures of latency (response speed) and percentage of correct responses. Match To Sample (MTS): A two-stimuli visual discrimination and category achievement test (Egerhazi et al., 2007) with outcome measures of mean correct reaction time, mean correct movement time and number of correct responses. The CANTAB offers four parallel versions of the MTS task to facilitate repeated testing. The four parallel tests were randomised across trials in order to reduce the influence of practice effects on this task. Stop Signal Task (SST): This task measures the ability to inhibit a pre-potent response. The stop-signal reaction time (SSRT; i.e., the processing time required to inhibit a pre-potent motor response), proportion of successful stops, and the number of direction errors made (incorrect button press) are calculated for each subject on the basis of these behavioural data (Yun et al., 2011). Stop Signal Reaction Time is an estimate of the length of time between the go stimulus and the stop stimulus at which the participant is able to successfully inhibit their response on 50% of trials. This measure is calculated from the SST RT on GO trials measure (reaction time on GO trials) and the SST SSD (50%) measure (stop signal delay at which the participant was able to stop 50% of the time, calculated as the arithmetic mean of the measured SSD from completed assessment stop trials) (Band et al., 2003). Stockings of Cambridge (SOC): This task is similar to the 'Tower of London' test and assesses spatial planning, which gives a measure of executive function (Egerhazi et al., 2007). Measures of performance are assessed for the number of trials completed in the minimum number of moves and the number of moves required to complete n move problems (where *n*=2, 3, 4 or 5).

Statistical Analysis

All statistical procedures were performed using SPSS for Windows, Version 19.0 (SPSS Inc., Chicago, IL). Statistical analysis for each of the main dependent variables on CANTAB tasks was conducted using paired samples *t*-tests to compare Test 1 and Test 2 responses for each trial. Pearson correlation coefficients (*r*) between performances on each assessment were taken as measures of test-retest reliability. Statistical significance was accepted at *p*<0.05. All data are reported as mean±standard deviation.

4.4.4 Results

Practice Effects

Mean results for each of the CANTAB assessment tasks is shown in Table 4.4a. There was a significant reduction in reaction time observed at re-test on the MTS task (*p*<0.05), indicating some effect of practice on performance in this task. No significant differences were observed on any of the other CANTAB assessment measures.

Table 4.4a. Analysis of practice effects in selected CANTAB tasks (*n* = 10)

CANTAB Task	Assessment	Test 1 Mean (SD)	Test 2 Mean (SD)	*t* Test	
				t value	*p* value
CRT	latency (*ms*)	253 (15)	258 (18)	-1.508	NS
	% correct	99.4 (0.7)	99.5 (0.5)	-0.557	NS
MTS	mean correct MT (*ms*)	550 (245)	505 (179)	0.850	NS
	mean correct RT (*ms*)	2054 (461)	1645 (309)	3.360	0.008
	% correct	94.4 (6.9)	95.6 (4.4)	-0.612	NS
SST	no. of direction errors	3.6 (4.0)	4.3 (5.7)	-0.639	NS
	mean correct RT (*ms*)	378 (58)	372 (80)	0.432	NS
	SSRT (*ms*)	148 (40)	137 (35)	1.444	NS
SOC	no. problems solved in min. moves	9.5 (1.8)	10.0 (1.6)	-1.000	NS
	no. moves for *n* = 4 task	5.4 (1.1)	5.2 (1.2)	0.390	NS
	no. moves for *n* = 5 task	6.1 (1.0)	5.9 (1.1)	0.930	NS

CRT – Choice Reaction Time, MTS – Match to Sample, SST – Stop Signal Task, SOC – Stockings of Cambridge, RT – reaction time, MT – movement time, SSRT – stop signal reaction time, NS – not significant (*p*>0.05).

Test-retest reliability

Test-retest correlation coefficients for each of the CANTAB assessment tasks are shown in Table 4.4b. Correlations were significant for several CANTAB outcome measures (CRT latency, MTS movement time, SST direction errors, reaction time and SSRT, SOC *n*=5 move task). However, correlation coefficients for some outcome measures (CRT % correct, MTS reaction time, MTS % correct, SOC problems solved in minimum moves and SOC *n*=4 move task) fall below the proposed ideal test-retest reliability range of 0.75-0.8 or above (Coolican, 2004).

Table 4.4b. Test-retest reliability of selected CANTAB tasks

CANTAB Task	Assessment	Correlation	
		r	*p* value
CRT	latency	0.76	0.011
	% correct	0.60	NS
MTS	mean correct MT	0.73	0.017
	mean correct RT	0.56	NS
	% correct	0.57	NS
SST	no. of direction errors	0.80	0.006
	mean correct RT	0.81	0.004
	SSRT	0.79	0.007
SOC	no. problems solved in min. moves	0.58	NS
	no. moves for *n* = 4 task	0.22	NS
	no. moves for *n* = 5 task	0.69	0.027

CRT – Choice Reaction Time, MTS – Match to Sample, SST – Stop Signal Task, SOC – Stockings of Cambridge, RT – reaction time, MT – movement time, SSRT – stop signal reaction time, NS – not significant (*p*>0.05).

4.4.5 Discussion

This study investigated the test-retest reliability of four tasks from the CANTAB testing instrument, administered on two occasions separated by several hours in the same day. The main aim of the study was to examine the influence of practice effects and time of day effects on the test-retest reliability of the selected CANTAB tasks. The results from this study indicate that there are no significant practice effects on any of the measured variables for the CRT, SST and SOC tasks. There was a significant reduction in reaction time on the MTS task, however no influence of practice was observed on movement time or the number of correct responses made for this task.

The reduction in reaction time on the MTS task may reflect the adoption of different strategies when completing this task in the second assessment. Lowe & Rabbitt (1998) observed similar results for the MTS (four choice) task in their study. However, they had elderly participants categorised into high and low ability groups and only found that MTS reaction time improved in the high ability group. Collectively this suggests that when the participants are capable, they are able to adopt strategies that may enhance their reaction time performance on repeated tests of this nature.

Several tasks demonstrated moderate to high test-retest reliability levels. Tasks involving low executive demand such as the CRT and SST had greater test-retest reliability compared to tasks requiring higher executive demand (i.e. SOC task) where improvements in task performance are typically strategy driven. Interestingly, high reliability was observed for CRT latency (r = 0.76) whilst only moderate reliability was achieved for the number of correct responses made on this task (r = 0.60). Participants may adopt different strategies on simple tasks such as CRT that ultimately results in a speed-accuracy trade off (Rabbitt & Vyas, 1970). That is, some participants may choose to increase speed at the expense of making more errors whilst others slow down their response speed to ensure greater accuracy is maintained. This can influence the test-retest reliability of the task and often results in one of the measured variables having a high correlation with the other being reduced (Lowe & Rabbitt, 1998).

Moderate test-retest reliability was observed with most of the measured variables from the MTS and SOC tasks (except the n=4 move task). Lowe & Rabbitt (1998) found similar results with the SOC task (called the Tower of London Task) in their study. However, contrasting results were found for the MTS task compared to that of the current study, with high correlation coefficients observed in their group for all levels of task difficulty. It should be noted, however, that the authors conducted the study with older adults (mean ~67 years), using a test-retest interval of four weeks and with the CANTAB tasks performed in a randomised order, which may explain the

differences in results between the studies. The moderate test-retest reliability found with the MTS and SOC tasks in the current study suggests that care must be taken when interpreting results if these tasks are used in future studies involving relatively brief test-retest intervals.

Many neuropsychological tasks involve examination of executive functioning or frontal lobe function and a key feature of these tasks is that they are only valid when they are novel (Lowe & Rabbitt, 1998). These tasks typically assess the ability to interpret and manipulate information, develop and apply strategies, monitor performance and plan ahead. Therefore, it may be expected that these types of tasks have poorer test-retest reliability as the novelty of the task decreases with repeated administration (Lowe & Rabbitt, 1998). Stability coefficients for CANTAB's measures of executive function in adult samples have been shown to be moderate in magnitude and generally range from 0.60 to 0.70 (Lowe & Rabbitt, 1998). The moderate test-retest reliability of executive function tasks implies that these tasks are associated with a rather large degree of variability over time. Consequently, changes in performance may be expected in repeated testing. However, this may simply reflect a common feature of these tests.

Whilst the use of the CANTAB testing instrument is well supported for neuropsychological assessments, there may be some limitations for its use in studies that employ brief test-retest intervals based on the data collected in this study. However, it must be emphasised that the present study was conducted using a small sample size (n=10), which reduces the overall power of the results. Typically, studies of test-retest reliability for neuropsychological tasks involve large sample sizes (n=100-200) (Lowe & Rabbitt, 1998; Bird et al., 2003). In light of these findings, the current study reinforces the importance of investigating the test-retest reliability of cognitive tasks intended for use in randomised control trials of cognitive performance, and emphasises that care must be taken when interpreting results where brief test-retest intervals have been employed.

In summary, the present study investigated the test-retest reliability of four tasks from the CANTAB testing instrument. The CRT and SST tasks showed excellent test-retest reliability, whilst

the MTS and SOC tasks showed only modest test-retest reliability. Computerised neuropsychological test instruments are valuable resources for measuring cognitive performance changes in research. However, findings from the present study suggest that some tests within the CANTAB battery may not meet the proposed ideal level of reliability to make repeated assessments and care should be taken when interpreting results from these tests. The CANTAB tasks employed in this study will be implemented in Research Study Three (Chapter Seven) to investigate the combined effects of dehydration and alcohol consumption on discrete measures of cognitive function.

4.5 Pilot Study Four - Test-Retest Reliability of Simulated Driving Performance

Reader's Note:

The information in this section has been published as an original research paper:

Irwin C, Shum D, Leveritt M, Desbrow B. Test-Retest Reliability of Simulated Driving Performance: A Pilot Study. *Proceedings of the Seventh International Driving Symposium on Human Factors in Driver Assessment, Training and Vehicle Design*, 2013; Bolton Landing, New York:p285-291.

The co-authors of this publication confirm that the research candidate has made the following contributions to this study:

- Developed the study design.

- Completed the human research ethics application.

- Designed and pilot tested the driving simulator scenarios.

- Conducted all participant recruitment and data collection.

- Conducted analysis of the data.

- Prepared manuscript for submission to the symposium.

- Presented research at an international conference.

Signed: _____   **Date: 06/09/13**

Signed: _____   **Date: 06/09/13**

Signed: _____   **Date: 06/09/13**

4.5.1 Abstract

Aim: To examine the test-retest reliability of assessment measures recorded during a naturalistic drive using a computerised simulated driving task. **Methods:** Twenty-seven volunteers completed three simulated driving tests to determine test-retest reliability of performance on a low-cost, fixed-base computerized driving simulator. One retest was completed a few hours after the initial drive, and the final retest was completed seven days following the initial test drive. Driving performance was compared using measures of vehicle control, speed and reaction time to critical events. A measure of participants' ability to inhibit a pre-potent response was also assessed using an inhibition task during each drive, with the number of incorrect inhibition responses recorded. **Results:** Practice effects were evident for measures of vehicle control (deviation of lane position and number of line crossings) and participants' ability to withhold responses to inhibition tasks. Good test-retest reliability was observed for measures of vehicle control, speed, reaction time and variability measures. Poor test-retest reliability was observed for the number of stopping failures observed during driving. **Conclusions:** The findings from this study suggest that the driving scenario used provides reliable assessment tasks that could be used to track the effects of pharmacological treatments on driving performance. However, an additional or longer familiarisation drive should be included as part of future study protocols employing this driving scenario to reduce learning effects during trials. Care should also be taken when interpreting results from tasks with low test-retest reliability.

4.5.2 Introduction

Driving simulators offer a safe and cost effective method of collecting objective and repeatable measures of driving performance (Allen et al., 2011). They also provide a means to investigate situations that would otherwise be dangerous (e.g. alcohol impaired driving, sleep deprived driving) (Caird & Horrey, 2011). Test-retest reliability of assessment instruments is important in behavioural based research and is a well-established principle in most areas of psychology. A substantial body of literature exists on the test-retest reliability of standardized neuropsychological assessments (e.g. Wisconsin Card Sorting Test). However, surprisingly few studies have examined the test-retest reliability of driving simulator measures (Törnros, 1998; Marcotte et al., 2003; Akinwuntan et al., 2009; Bedard et al., 2010). In those that have, the repeated administration of driving tests appears to follow after a significant time lapse (2-3 months). Laboratory based studies of driving behaviour and performance often involve multiple assessments of individuals. For example, when investigating pharmacological effects (e.g. alcohol) on driving performance, researchers often employ protocols that involve testing before and after exposure to a treatment. In these cases, the duration between initial testing and retesting is likely to be a matter of minutes or hours rather than months. There are implications for the use of

assessment tasks that have low test-retest reliability in applied or clinical settings. They are limited in the test's sensitivity to detect changes in performance when administered repeatedly (Lowe & Rabbitt, 1998). A limitation of repeated testing is that improvement with practice may occur (Beglinger et al., 2005). This is normally most pronounced when intervals between testing are short and could potentially mask other effects that may be present, leading to confounding results (Collie et al., 2003). The purpose of this pilot study was to examine the test-retest reliability of driving simulator performance measures over relatively short re-test intervals (hours and days). Test-retest reliability data from this study may provide greater confidence in the interpretation of driving performance changes observed in future studies where retesting is completed after short delay intervals and treatment effects are anticipated.

4.5.3 Materials and Methods

Participants

Twenty-seven volunteers (13 male, 14 female) aged between 19 and 34 yrs (mean 24.5±4.4 yrs) participated in this study. Participants had no known neurological conditions or injuries that would influence their driving ability. All participants held a valid driver's license, had at least two years driving experience (range 2-18 yrs), and drove at least 5000 km each year.

Experimental Procedures

For each testing session, participants were asked to refrain from alcohol, non-prescription medications, and recreational drugs in the 24hrs prior to each test. In addition, they were asked to avoid consuming any caffeinated food and beverages and to drink at least one litre of water in the two hours prior to testing to assist with maintaining adequate hydration status. Dehydration has been associated with impairment in cognitive functions and mood, which may influence driving performance (Grandjean & Grandjean, 2007; Lieberman, 2010). Prior to completing the

experimental drives, all participants completed a 10 min familiarisation drive on the simulator to become accustomed to the controls and driving in the virtual environment. Two of the experimental drives were conducted on the same day, one completed between the hours of 08:00 and 11:00 (Test 1), and one completed between the hours of 13:00 and 16:00 (Test 2). The third experimental drive was conducted approximately seven days after the initial test drive between the hours of 10:00 and 14:00 (Test 3).

Experimental Drives

The driving simulation task was operated on a desktop computer with peripheral devices for steering wheel, gas and brake pedals and gear shifter (Figure 4.5a). Visual images were displayed on three 22-inch LCD monitors (3840 x 1024 resolution), set to provide a 100° front field of view. A rear scene was also displayed on the central monitor to provide images associated with the rear view mirror. Images from the simulation software were refreshed at a rate of 60Hz, with data sampled at a rate of 20Hz. Auditory and haptic feedback were provided using a stereo sound system and force feedback steering. Kinematic and behavioural data of the controlled vehicle was recorded by the simulator's software program and converted to a spreadsheet data set allowing analysis of mathematical determinants from the vehicle. The simulation display provided a view of the road and vehicle dashboard instruments (Figure 4.5b).

Fig. 4.5a. Driving simulator set-up**.**   **Fig. 4.5b.** Visual simulation display.

The simulated vehicle was set to automatic transmission. Participants were instructed to stay in the centre of the left-hand lane and adhere to all normal road rules and speed signs. A GPS provided audio and visual (arrow) directions for the itinerary. Crashes into other vehicles would result in the presentation and sound of a shattered windshield. The program then reset the car in the centre of the left lane at the point of the crash and allowed the participant to resume driving.

In the experimental drives, participants completed a 10 km course, which took approximately 15 min. The driving scenario was set in daylight conditions and comprised six main sections (Table 4.5a). Other vehicles and pedestrians were present in the scenario but did not actively interact with the participant's vehicle. The experimental drives were intended to assess naturalistic driving performance in order to increase the application of the investigation to real-world driving. As such, participants were given minimal instructions on how to drive during the scenarios, and were provided no task priorities, incentives or performance feedback.

Table 4.5a. Driving simulator scenario for experimental drives

Section	Description	Length (Km)	Configuration	Critical Events
1	Re-familiarisation	3.00	2 lane single carriageway. 50, 80 & 100km/hr sign posted sections. 2 intersections with traffic signals, 1 intersection with stop sign. Few buildings and lightly landscaped areas. Light traffic present.	2 RI + 2 RT events
2	Highway 1	0.55	2 lane single carriageway. 80km/hr sign posted section. Few buildings and lightly landscaped areas. Light traffic present.	1 RI event
3	City 1	0.70	4 lane dual carriageway. 50km/hr sign posted section. 5 intersections with traffic signals. Many buildings and highly landscaped areas. Moderate traffic present.	1 RT event
4	Rural / Suburban	2.20	2 lane single carriageway. 50km/hr sign posted sections. 4 intersections with traffic signals, 1 intersection with stop sign. Few buildings and lightly landscaped areas. Light traffic present.	1 RI + 2 RT events
5	Highway 2	2.60	2 lane single carriageway. 80 & 100km/hr sign posted sections. 1 intersection with traffic signal. Few buildings and lightly landscaped areas. Light traffic present travelling in opposite direction.	1 RI + 1 RT + 1 Headway* event
6	City 2	0.95	4 lane dual carriageway. 50km/hr sign posted sections. 4 intersections with traffic signals. Many buildings and highly landscaped areas. Moderate traffic present.	2 RI + 1 RT events

Note: example of critical events provided is from test scenario 1. Parallel versions of test scenarios may have differed in arrangement of critical events. RI – response inhibition event, RT – reaction time event. * Headway event occurred in a section separate from RI and RT events. Light traffic – may encounter 2-3 other vehicles, Moderate traffic – may encounter 6-8 other vehicles.

Reaction Time Events

During each experimental drive, participants were required to respond to stimuli on five occasions in order to test reaction time (RT). For each reaction time event, the stimulus was the presentation of a stop signal image on the right side of the centre screen. Participants were instructed to brake as quickly as possible when the stimulus appeared. Once they had come to a complete stop, the stimulus disappeared from view and participants could resume driving.

Response Inhibition Events

During the experimental drive, participants were presented with a response inhibition task on five occasions. For each event, a stop signal image was presented on the right side of the centre screen. A short auditory tone was played after a 400 ms delay on visual presentation of the stimulus. Participants were instructed to withhold their usual brake response to the stop signal stimulus if they heard the auditory sound. This test provided a measure of participants' ability to inhibit a pre-potent response and the total number of incorrect inhibition responses (IIR) were recorded.

Headway Events

On one occasion during the experimental drive, participants encountered a vehicle placed on the road ahead of them travelling at a speed set at 10 km/hr below the designated speed limit (100 km/hr). This event was set to occur at a pre-defined location in each test drive scenario. The road was a single carriageway section with solid centre line markings to avoid having the participant overtake and pass the vehicle. The lead vehicle was present for the headway event until the next intersection and required participants to follow for a total distance of 1.5 km. This event was used to examine participants' car following behaviour, with time to collision (TTC) between the interactive vehicle and back of the vehicle ahead measured for the duration of the

following task. Participants were not provided with any instructions on how close to follow the lead vehicle.

Red Traffic Signals and Stop Signs

During the experimental drives, participants encountered 15 intersections. One intersection had a stop sign and required the driver to stop completely before resuming driving and passing through the intersection. The other 14 intersections were equipped with traffic lights. At five of the intersections, the traffic light was red and required the driver to stop until the light turned green. At three intersections the traffic light was green and did not require the driver to stop. At the remaining six intersections, the light turned from yellow to red as the vehicle approached with enough time and distance for the driver to stop at the intersection. Order of the traffic lights was randomly allocated throughout each test drive scenario. Failing to stop at intersections with the stop sign, red traffic lights and traffic lights that changed from orange to red as the vehicle approached were recorded as a failure to stop performance measure (total stops required = 12).

Other Driving Performance Measures

Several other measures of driving performance were obtained during the experimental drives. Table 4.5b provides a list and description of each of the other performance variables recorded. The driving aspects that were measured were chosen on the basis of their established sensitivity to the disruptive effects of alcohol as demonstrated in previous research (Fillmore et al., 2008). These measures provide a method of assessing vehicle control and violation of driving regulations, which are associated with driving safety and increased risk of traffic accidents (Retting et al., 2003; Verster & Roth, 2011).

Table 4.5b. Driving simulator performance measures

Performance Measure	Description
Avg. Speed	Average speed throughout the driving scenario.
SDLP	Standard deviation of the driver's average within-lane position.
SDSA	Standard deviation of steering angle.
LC	When the interactive vehicle moved outside the lane, either crossing the centre line into the oncoming traffic lane (centre line crossings) or crossing the road shoulder (side line crossings). The total number of line crossings was recorded.
Off road and other vehicle impacts	The number of off-road crashes (with objects in the environment) and impacts involving other vehicles during the test.
FTS	The number of times a participant failed to stop at a red traffic light or road stop sign throughout the test.

Statistical Analysis

All statistical procedures were performed using SPSS for Windows, Version 19.0 (SPSS Inc., Chicago, IL). Differences between trials for each of the main dependent variables in the driving task were examined using one-way repeated measures ANOVA. Pair-wise comparisons (Bonferroni) were performed where significant main effects were present. Effect size was reported as partial eta squared (η_p^2). Intra-class correlation coefficients (ICC) were calculated using the two-way mixed average measures (absolute agreement) model. Coefficients of variation for each of the driving performance measures representative of continuous data were calculated by standard methods using the mean and standard deviations of each variable across the three trials. Statistical significance was accepted at $p < 0.05$. All data are reported as mean±standard deviation.

4.5.4 Results

All participants completed the three test drives with no complications or simulator sickness reported. Off road and other vehicle impacts were extremely rare ($n=2$), thus precluding any statistical analyses. Mean results for each experimental drive are shown in Table 4.5c. There was a significant reduction in lane position deviation observed in Test 3 compared to Test 1 ($p < 0.05$).

Participants had more line crossings in Test 1 compared to the two subsequent tests ($p<0.05$), and a reduction in the number of incorrect inhibition responses (braking when a stop signal stimulus and inhibitory auditory tone was present) was observed in Test 3 compared to Test 1 and Test 2 ($p<0.05$). No difference was seen in performance on this task between Test 1 and Test 2 ($p>0.05$). No significant differences were observed between tests for any of the other driving performance measures assessed ($p>0.05$).

Table 4.5c. Analysis of practice effects in repeated driving performance tests

Performance Measure	Test 1 mean (SD)	Test 2 mean (SD)	Test 3 Mean (SD)	ANOVA F (2, 25)	Sig	η_p^2
Avg. speed (Km/hr)	42.72 (1.82)	43.13 (2.24)	43.35 (1.51)	2.580	ns	0.17
SDLP (m)	0.35 (0.06)	0.34 (0.05)	0.33 (0.05) *	4.041	$p<0.05$	0.24
SDSA (deg)	0.77 (0.07)	0.77 (0.06)	0.77 (0.06)	0.102	ns	0.01
TTC (s)	2.78 (1.28)	2.92 (0.96)	2.73 (1.07)	0.531	ns	0.04
LC (*n*)	5.93 (4.57)	4.44 (3.67) *	3.78 (3.52) *	9.998	$p<0.05$	0.44
RT (s)	0.96 (0.11)	0.94 (0.11)	0.95 (0.14)	1.286	ns	0.09
FTS (*n*)	0.07 (0.27)	0.22 (0.51)	0.11 (0.32)	0.792	ns	0.06
IIR (*n*)	1.67 (1.21)	1.96 (1.51)	0.67 (1.11) **	13.590	$p<0.05$	0.52

* Significant difference compared to Test 1 ($p<0.05$), ** Significant difference compared to Test 1 and Test 2 ($p<0.05$).

Significant moderate to high ICCs were found for most assessment measures, indicating good to excellent reliability (Table 4.5d). However, ICC values for the number of failures to stop outcome measure show low levels of test-retest reliability. The degree of variability in individuals' performance across driving tests was determined using coefficient of variation (CV). A low degree of intra-individual variability was observed for all performance measures except TTC performance.

Table 4.5d. ICC and CVs for three experimental drives

Performance Measure	ICC	95% CI	CV (%)
Avg. speed	0.69*	0.43 - 0.85	2.4
SDLP	0.92*	0.84 - 0.96	5.7
SDSA	0.91*	0.83 - 0.96	2.9
TTC	0.77*	0.56 - 0.89	17.7
LC	0.88*	0.75 - 0.95	-
RT	0.74*	0.51 - 0.88	6.9
FTS	-0.47	-1.80 - 0.28	-
IIR	0.47*	0.06 - 0.73	-

* Significance at the $p<0.05$ level.

4.5.5 Discussion

Overall, most of the driving performance measures in this study demonstrated moderate to high test-retest reliability. Participants were able to maintain consistent speed, vehicle control (lane position, steering angle), and response time to critical events across repeated tests. Similar to previous work by Tornros (1998) and Marcotte et al. (2003), high test-retest reliability was observed for speed and lane position. The results also support the work of Akinwuntan et al. (2009) who observed high test-retest reliability for reaction time responses during driving. Whilst a high ICC coefficient was observed for TTC to lead vehicles indicating high test-retest reliability, the high CV value for this variable suggests a large intra-individual variation in car following behaviour. Recent work by Brackstone et al. (2009) suggests that drivers are inconsistent in their choice of headway, with individual variations above 19% in adopted headway observed between trials in their study. Collectively, these results suggest that driving headway is likely to be susceptible to intra-individual differences. A low ICC coefficient was observed for the number of stopping failures in this study. Given these findings, this may have implications for the use of this measure as a performance variable in future studies. However, given that there were very few stopping failure instances across all three drives it is possible that decision errors or misjudgements by participants

(they thought they could clear the intersection before the red light but failed) explain the observed differences and low reliability.

In the present study there did appear to be some influence of practice on a number of performance measures. Lane position deviation was lower in drive three compared to drive one. In addition, the total number of line crossings was higher in the initial test drive compared to the subsequent drives. Whilst participants completed a single familiarisation drive prior to the test drives, these results suggest that inclusion of an additional familiarisation drive may help to reduce any learning effect. Participants also had a greater ability to correctly withhold their brake response to inhibition stimuli in the final test drive compared to the first two drives. However, a true practice effect would assume directional change as trials progressed. Participants made fewer incorrect inhibition mistakes in the final drive compared to the first and second drives, yet an increase was observed from drive one to drive two. A possible explanation for these results may relate to the type of task used. Response inhibition tasks involve a reaction component in addition to a measure of accuracy. As such, participants may adopt different strategies that ultimately result in a speed-accuracy trade off (Rabbitt & Vyas, 1970). Reaction time for brake pedal press during the response inhibition task was not measured in this study, but may explain the differences observed between trials. It is possible that participants adopted strategies on the final test drive where speed of response was forfeited to allow fewer errors to be made. Further investigation of test-retest reliability for response inhibition tasks during simulated driving are needed to clarify these results.

One of the limitations of this study is that compliance to pre-experimental conditions was verbally acknowledged. These would be better verified with objective measures (e.g. breath analysis for alcohol, plasma analysis for caffeine). In addition, it is important to acknowledge that this study involved a desktop computer based simulator and it is likely that larger, very-high fidelity simulators with greater fields of view are more realistic of real world driving and may be

more sensitive to the measures assessed in this study. The test-retest reliability results presented in this study are based on the equivalent absence of differences between test drives. Conclusions may have been strengthened if the effects of a treatment (e.g. alcohol consumption) had been shown to be consistent across repeated testing, thus demonstrating equivalent sensitivity of effects rather than the equivalent absence of differences. Finally, this study involved a naturalistic drive and participants were given minimal instructions on how to drive during the scenarios, providing no task priorities, incentives or performance feedback. More traditional testing protocols typically involve a highly constrained situation in which test participants have little freedom to choose responses. Driving behaviour is different, particularly when it is relatively unconstrained and the absence of differences between some metrics measured in this study may be due to relatively high levels of variability. The use of a driving simulator protocol with more constrained instructions may be better for the purpose of measuring test-retest reliability, reducing driving variability.

In summary, the findings from this study suggest that the driving scenario used provides assessment tasks that may be reliable for tracking the effects of pharmacological treatments on driving abilities, when test-retest assessments are made following relatively short delay periods. However, an additional or longer familiarisation drive should be included as part of future study protocols employing this driving scenario to reduce learning effects during trials. Care should also be taken when interpreting results from tasks with low test-retest reliability. The driving scenarios developed in this study will be used to examine the combined effects of dehydration and alcohol consumption on driving performance in Research Study Four (Chapter Eight).

Chapter Five: Research Study One - Industrial Workers' Hydration: Attitudes, Perceptions and Practices Regarding Post-Shift Alcohol Consumption

Reader's Note:

The information in this section has been published as an original research paper:

Irwin C, Leveritt M, Desbrow B. A Hard Earned Thirst: Workplace Hydration and Attitudes Regarding Post-Shift Alcohol Consumption. *Journal of Health, Safety and Environment*, 2013; 29(1):p51-67.

The co-authors of this publication confirm that the research candidate has made the following contributions to this study:

- Developed the study design.

- Completed the human research ethics application.

- Designed and pilot tested the semi-structured interview questions.

- Conducted all participant recruitment, hydration assessments and participant interviews.

- Transcribed the interview recordings.

- Conducted thematic analysis and participated in discussions for confirmation of themes.

- Prepared manuscript for submission to journal.

Signed: _____   **Date: 06/09/13**

Signed: _____   **Date: 06/09/13**

5.1 Abstract

Aim: Industrial workers are often challenged by hydration issues, and may consume alcohol after a day at work. The consumption of alcohol in a dehydrated state could impose significant health and safety concerns for these individuals. **Methods:** In this study, the hydration status of 16 male industrial workers (age: 39.3±8.3 yrs, mean±SD) was monitored by measuring U_{sg} over two consecutive days at work, prior to exploring attitudes, perceptions and practices towards alcohol consumption using a semi-structured telephone interview. **Results:** Urine sample analysis indicated that 33% of workers were inadequately hydrated ($U_{sg} > 1.020$) at the beginning of the shift and 24% of workers were inadequately hydrated at the end of the shift on day one. On day two, 41% of workers were inadequately hydrated at the beginning of the shift and 31% of workers were inadequately hydrated at the end of the shift. The majority of workers believed alcohol consumption after work was acceptable, and indicated a lack of consideration for hydration levels prior to consuming alcohol. **Conclusions:** Further research is required in order to gain a better understanding of hydration in the workplace and workers' attitudes and behaviours towards post-shift fluid consumption (including alcohol). This may assist with the development of appropriate public health campaigns highlighting the implications of alcohol consumption in situations where dehydration is anticipated.

5.2 Introduction

Maintenance of TBW balance is essential for practically all functions of the body (Jequier & Constant, 2010). The regulation of fluid intake is multi-factorial, and is thought to involve an integration of neural and hormonal signals that generate the thirst drive (McKinley & Johnson, 2004). However, the initiation of thirst is delayed in response to body fluid losses and typically occurs when ~1-2% of body weight (as fluid loss through sweating) has been lost (Miller & Bates, 2007). This level of dehydration has been associated with adverse effects on physical and mental functions (Grandjean & Grandjean, 2007; Sawka et al., 2007; Shirreffs, 2009; Lieberman, 2010).

Industrial workers are often challenged by hydration issues (Kenefick & Sawka, 2007). These individuals may perform intense physical labour in warm-hot environments, promoting sweat outputs that exceed water intake, leading to body water deficits or dehydration (Kenefick & Sawka, 2007). Several studies have investigated the prevalence and severity of dehydration across a range of industrial facilities (Kampmann et al., 1998; Bates et al., 2001; Parker et al., 2001, 2002; Brake & Bates, 2003; Carter et al., 2006; Morioka et al., 2006; Carter & Muller, 2007; Miller & Bates, 2007; Bates & Schneider, 2008; Bates et al., 2010; Biggs et al., 2011; Hunt et al., 2011). Manual work in warm conditions can promote sweat rates exceeding 1.0 L/hr (Miller & Bates, 2007; Bates & Miller, 2008). During prolonged periods of physical exertion (8-12hr shifts) this can

result in large volumes of fluid loss (Bates & Schneider, 2008). Additional factors such as environmental conditions, physical activity levels, clothing and equipment can exacerbate these fluid losses. Sweat rates above 2.0L/hr have been observed in simulated industrial work conditions when protective clothing is worn (Bishop et al., 1991; Kenefick & Sawka, 2007). Furthermore, it is well documented that workers may not only become dehydrated on the job, but also start the work day in fluid deficit (Kenefick & Sawka, 2007; Miller & Bates, 2007; Bates & Miller, 2008). Dehydration reduces physical work capacity and lowers heat tolerance (Murray, 2007). Individuals that are dehydrated prior to starting work are more susceptible to developing heat related illness as work conditions become increasingly stressful (Clapp et al., 2002).

Maintaining TBW balance during physical exertion is essential for the health and safety of industrial workers (Kenefick et al., 2003), and is also important for optimal performance and productivity at the work site (Bates & Schneider, 2008). Dehydration that causes deterioration in cognitive performance may have safety implications for industrial workers that operate machinery or motor vehicles, and for the safety of individuals around them (Grandjean & Grandjean, 2007; Lieberman, 2007). Not surprisingly, workplace accidents and injuries are more common in hot environments, and are often associated with dehydration (Bates & Schneider, 2008). This may have significant economic impact with workplace accidents and injuries contributing to increased health care costs and reduced industrial earnings through lost productivity (Kenefick & Sawka, 2007). More importantly, however, is the great personal cost (loss of income, disabling injury, death etc.) that may occur as a result of accidents or injuries at work.

Industrial workers are among the occupational groups that have the highest proportion of full-time employees that consume alcohol (Zhang & Snizek, 2003). There is some evidence to suggest that adverse occupational working conditions may be partly responsible for this, with workers using alcohol as a coping mechanism for harsh working conditions and to aid relaxation (Zhang & Snizek, 2003). A number of sociological studies have also described alcohol consumption among

industrial-type workers as being part of the occupational culture (Janes & Ames, 1989; San José et al., 2000; Zhang & Snizek, 2003; Berry et al., 2007). In some cases alcohol may be consumed after physical exertion that results in fluid loss and where insufficient rehydration has occurred. The consumption of alcohol under conditions of mild or moderate dehydration may influence individuals' willingness to take risks more so than under conditions where fluid deficit is not present. This may result in increased incidences of injury and harm through alcohol mediated risk-taking behaviour (i.e. driving under the influence). In addition, alcohol may compromise rehydration (Eisenhofer & Johnson, 1983), which could lead to alcohol hangover and subsequent increased rates of absenteeism and poor job performance (Wiese et al., 2000).

It is important for industrial workers to restore TBW balance following work, because they are often required to complete consecutive shifts over a number of days (Clapp et al., 2002). However, behaviour away from the workplace may have an important influence on hydration levels (Carter et al., 2006; Carter & Muller, 2007). Rehydration strategies before and after work shifts are critical to restoration of TBW balance (Biggs et al., 2011). Inappropriate rehydration strategies may be influenced by the availability and appeal of beverages that often hinder rehydration (Clapp et al., 2002; Kenefick et al., 2003; Zhang & Snizek, 2003; Berry et al., 2007; Lieberman, 2007; Bates & Miller, 2008), including alcohol, and the limited contribution these beverages play in rehydration (Bates, 1996; Brake & Bates, 2003). Whilst many studies have examined the hydration practices and status of workers throughout the work shift, few have monitored rehydration practices outside of the workplace (Carter & Muller, 2007). There is also little evidence around factors that influence workers' fluid choices post-shift, particularly with regard to alcoholic beverages. Understanding workers' attitudes and perceptions toward alcohol consumption after work is an important step in defining factors that influence the overall health and safety of workers. This information may assist with the development of tailored and appropriate public health campaigns regarding social alcohol consumption in situations where dehydration is anticipated.

129

The aim of this study was to determine the hydration status of industrial workers over consecutive days at the job site, and explore typical post-work behaviours, attitudes and perceptions relating to alcohol consumption.

5.3 Materials and Methods

Experimental Design

This study used a mixed-methods approach to data collection. Quantitative methods were employed to determine the hydration status and self-reported fluid consumption of workers. Qualitative methods were used to explore perceptions of workers toward post-work rehydration behaviour, including alcohol consumption. Qualitative data collection was ceased when collection of additional data did not result in the identification of any new themes.

Participants

The study was carried out across two industrial sites located in the South-East Queensland region of Australia. Average conditions in this area during the months of January and February usually range between 21-27°C, and 70-80% relative humidity (Bureau of Meteorology, 2012). Volunteers from the two industrial sites were invited to participate in the study during an initial visit to each location. The study was open to all employees (male and female, all age groups) of the work site, with the only inclusion criteria for participation specifying that the employee was involved in some form of manual labour at the work site. Participants were aware that the study was investigating hydration status and behaviours, both at the work site and following the work shift. However, participants were not informed that the primary purpose of the study was to explore post-work behaviours, attitudes and perceptions relating to alcohol consumption.

Eighteen male employees, aged 39.3±8.3 yrs (mean±SD) volunteered to participate in the study. Two of the participants did not complete all of the measures taken over the course of the study,

resulting in complete data collection on 16 participants. At site one, participants were engaged in the manufacture of plasterboard based wall and ceiling lining systems, with work activities that included machine operation, light manual handling duties and some forklift operation. Employees at this facility worked in an enclosed factory area with no exposure to direct sunlight and completed a work roster consisting of two consecutive day shifts (from 06:00 to 18:00hrs), followed by two consecutive night shifts (18:00 to 06:00hrs), prior to four successive days off. At site two, participants were engaged in the construction of a large multi-story building with work activities that varied between light supervisory roles and heavy manual duties. Employees at this site worked mostly outdoors, with environments that ranged from below ground level to several floors above ground, and varied in terms of exposure to direct sunlight and air flow. Employees completed a work roster consisting of six consecutive 8-10hr day shifts (between 06:00 to 16:00hrs), followed by two consecutive days off. Of the 16 participants with complete data, the final shift was a Tuesday for $n=3$, a Wednesday for $n=4$, a Friday for $n=3$ and a Sunday for $n=6$. All volunteers gave written informed consent to participate in the study. Ethics approval for the study was granted from Griffith University's Human Research Ethics Committee (Protocol Number PBH/45/11/HREC).

Experimental Procedure

Research was conducted during the months of January and February in 2012. Each participant's hydration status was monitored over two consecutive day shifts, which were followed by a day off, as shown in Fig. 5a.
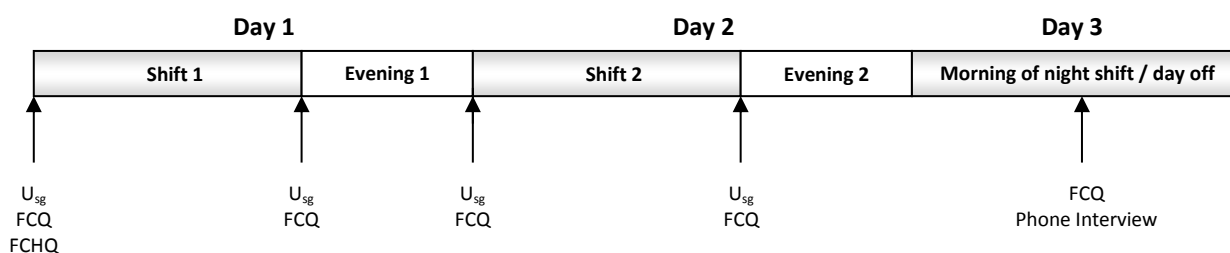
	Day 1		Day 2		Day 3
	Shift 1	Evening 1	Shift 2	Evening 2	Morning of night shift / day off

U$_{sg}$
FCQ
FCHQ

U$_{sg}$
FCQ

U$_{sg}$
FCQ

U$_{sg}$
FCQ

FCQ
Phone Interview

Fig. 5a. Experimental protocol. U$_{sg}$ – urine specific gravity assessment, FCQ – fluid consumption questionnaire, FCHQ – fluid consumption history questionnaire, Phone Interview – semi-structured questions related to attitudes and perceptions of post work rehydration.

Quantitative Data Collection

The hydration status of participants was assessed at the beginning and end of each shift from U$_{sg}$ using a digital refractometer (UG-α, ATAGO Co. Ltd, Tokyo, Japan). Urine samples were collected from participants immediately on arrival to the work site and again immediately following the end of the work shift, prior to the participant leaving the work site. Urine specific gravity has been widely adopted as a convenient and reasonably reliable index of hydration status in field settings (Armstrong, 2007). In humans, normal urine specimens have U$_{sg}$ values ranging from 1.013 to 1.029 g/ml. The U$_{sg}$ values recorded were grouped into hydration status categories based on previous definitions (Miller & Bates, 2007; Bates et al., 2010).

Fluid intake was assessed on work days (days one and two) at the beginning and end of the shift using a self-administered questionnaire. A 12hr dietary recall method was used to gather information regarding fluid type and volume for each participant. These methods have demonstrated reasonable reliability and validity, and are dependable for estimation of nutritional intake and for relative comparisons (Lennernas et al., 1995; Del Boca & Darkes, 2003). Participants were instructed to follow their normal behaviour regarding fluid intake for the two days of data collection, and on each fluid consumption questionnaire participants were asked to indicate if the intake was representative of normal daily behaviour using a 'yes' or 'no' response. Where relevant, participants were asked to describe uncharacteristic fluid intake behaviour. At the same time each questionnaire was administered, participants also completed a form containing eight

visual analogue scales (VAS), assessing subjective ratings of body symptoms. Each scale was presented as a 100mm line, the ends marked antonyms (very dehydrated-very hydrated, not very thirsty-very thirsty, no headache-severe headache, very cold-very hot, very dry mouth-very wet mouth, not light headed/dizzy-very light headed/dizzy, not sweaty-very sweaty, not able to concentrate-very able to concentrate), and participants placed a mark on each line to represent how they felt at that moment. The questionnaires administered at the end of each work day also asked participants to rate the physical intensity of the work shift on a five point Likert scale (very light, light, somewhat hard, hard, very hard). On day three, participants were contacted via phone to complete a fluid consumption questionnaire to determine intake after work the previous day.

Environmental conditions were monitored for each day of data collection (Kestral® 4200 Pocket Air Flow Tracker, Nielsen-Kellerman, Boothwyn, PA, USA) with recordings of ambient air temperature (T), relative humidity (RH), wet bulb globe temperature (WBGT), heat index (HI), and air flow (AF) taken every hour during the work shift. Heat index attempts to determine the human perceived equivalent temperature and is often used as a practical measure of how hot the current combination of RH and T feels to a human body (Rothfusz, 1990).

Statistical Analysis of Quantitative Data

All statistical procedures were performed using IBM SPSS for Windows, Version 20.0 (IBM Corp., New York, USA). One-way ANOVA was used to compare self-reported fluid intake of participants and subjective ratings of body symptoms from the VAS questionnaires. Participants were categorised into three groups based on hydration status (dehydrated, marginally-adequately hydrated and optimally hydrated) prior to conducting the ANOVA. The dehydrated category included all participants indicating U_{sg} readings >1.021. Pair-wise comparisons (LSD) were performed where significant main effects were present. Statistical significance was accepted at p<0.05. All data are reported as mean±standard deviation unless otherwise specified.

Qualitative Data Collection and Interview Design

After collection of fluid consumption data on day three, each participant took part in a semi-structured telephone interview to investigate the factors affecting fluid consumption at work, typical post-work rehydration behaviours, and attitudes and perceptions relating to alcohol consumption after work. Interview questions were developed using an inquiry logic reflecting the investigative aims of the study, as shown in Table 5a. Interviews were six minutes on average, with a range of three to nine minutes. Telephone interviews were audio-recorded and transcribed verbatim.

Table 5a. Interview guide and inquiry logic

Interview Questions	Inquiry Logic
Do you think there are any barriers to consuming enough fluid at work?	Describe factors affecting fluid consumption in the workplace.
What are your thoughts about drinking alcohol after work?	Describe attitudes of individuals towards alcohol consumption after work.
What sort of things influence whether you drink alcohol after work?	Explore perceived factors that influence alcohol intake after physical activity/exertion.
When you do have alcohol after work, do you ever think about your hydration levels before drinking?	Explore awareness of hydration as an issue prior to alcohol consumption after work.
Do you have anything else you would like to add on the topic of hydration and alcohol?	Other comments.

Data Analysis of Qualitative Data

Each interview was transcribed using indexing and partial transcription. The indexed transcriptions were thematically analysed using the constant comparison method, identifying trends and common ideas shared by interviewed participants (Strauss & Corbin, 1998). Thematic trends were coded, allowing for comparisons between interviews and triangulation of the themes was performed by an independent researcher. Selected passages of text from transcripts have been used to illustrate key themes identified from the data. Passages of text included in this paper

are followed by a participant number, which can be used to identify hydration parameters and alcohol consumption practices, as shown in Table 5b of the results section.

5.4 Results

Quantitative Data

Data collection occurred on eight days during the allocated study period. Five participants took part in the study over the first two days (data was incomplete for one participant), eight participants had data collected on them on days three and four (one of which was incomplete), three participants completed the study on days six and seven, and three participants completed the study on the final two days of data collection. The average rating of physical intensity of the work by participants completed throughout the data collection period was considered to be 'somewhat hard'. Over the two days for each data collection period, 11 workers rated their shifts as very light to light in intensity, 16 rated their shifts as moderately hard, and six rated the intensity of the shifts as hard to very hard.

Environmental Data

The environmental data collected over the study period indicated similar conditions across each of the data collection days. Average ambient temperatures ranged between a minimum of 25.3 ± 1.5°C to a maximum of 28.7 ± 1.8°C, with relative humidity between 68.9 ± 13.4% and 85.1 ± 5.7%. Average wet bulb globe temperature readings were between 23.0 ± 1.7°C minimum and 24.6 ± 1.2°C maximum. The ambient temperature and humidity readings translated to heat index values between 27.9 ± 2.8°C minimum and 32.7 ± 2.3°C maximum. No air flow was recorded on days one to six at the indoor factory site. Air flow at the outdoor construction site averaged between 3.5 ± 2.3 km/hr on the collection days.

Hydration Status

Urine specific gravity recorded for each individual across the two work days are shown in Table 5b. There was no obvious influence of work shift or subjective ratings of work intensity on hydration status. There were two accounts of dehydration when the work intensity was rated as very easy-easy, five accounts when the work shift was rated as moderately hard, and one account when the shift was rated as hard-very hard. Similar results in workers' hydration levels were observed across both days. The distribution of U_{sg} values for all participants is shown in Fig. 5b.

Table 5b. Urine specific gravity values recorded for each individual (n = 18)

Participant	U_{sg} Values			
	Day 1		Day 2	
	Beginning	End	Beginning	End
1	**1.022**	**1.023**	**1.023**	**1.023***
2	1.003	1.010	1.005	1.012
3	**1.023**	*1.020*	1.015	1.013
4	1.005	*1.019*	1.003	1.013
5	*1.020*	-	-	-
6	**1.028**	1.013	*1.020*	**1.022**
7	**1.021**	1.007*	**1.023**	1.009*
8	1.011	*1.018*	1.002	*1.020*
9	*1.017*	**1.026**	**1.024**	**1.026***
10	**1.022**	*1.019*	*1.017*	-
11	*1.016*	1.004	1.005	1.015
12	**1.024**	**1.022**	**1.022**	**1.024**
13	*1.020*	1.009	*1.018*	*1.019*
14	1.010	1.006	**1.023**	1.003
15	*1.016*	**1.021***	**1.022**	*1.019***
16	1.011	1.005*	1.015	*1.017***
17	*1.017*	1.013*	1.014	*1.016***
18	1.014	*1.020*	**1.024**	**1.024**
Total no. dehydrated	6	4	7	5

Note: **Values in bold font** indicate levels in the dehydrated category (U_{sg}>1.020), *Values in italic font* indicate levels in the marginally-adequately hydrated category (U_{sg}=1.016-1.020), Values in normal font indicate levels in the optimal level of hydration category (U_{sg}≤1.015), - indicates U_{sg} sample was not collected. * indicates that the participant consumed alcohol after the work shift.
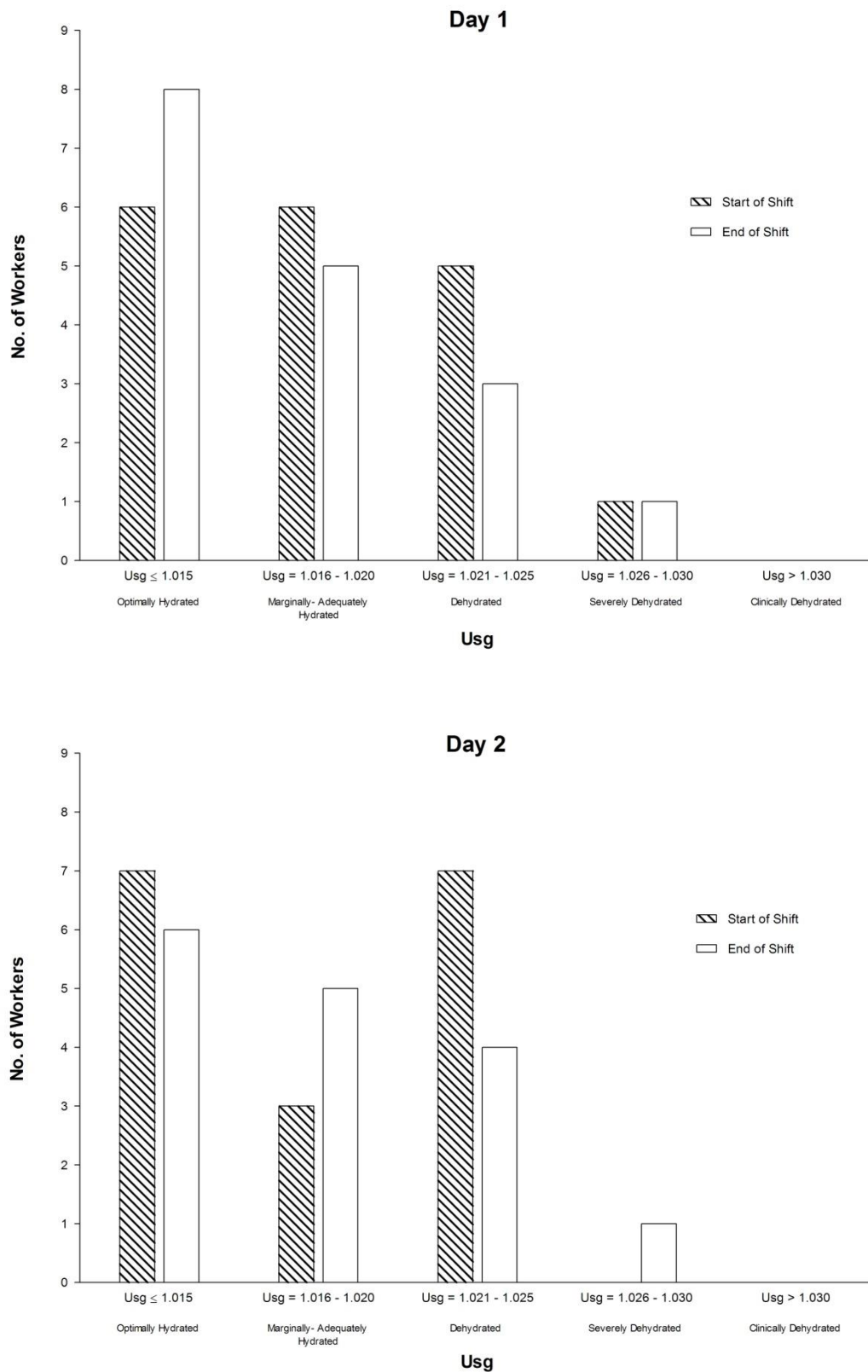
Fig. 5b. Change in hydration status on each day. Urine specific gravity values recorded at the beginning and end of the work shift (*n* = total of 68 samples over the two work days).

Self-reported Fluid Intake

Fluid intake reported by participants was acknowledged to be typical of normal drinking behaviour. All participants indicated a 'yes' response to the statement regarding normal fluid intake behaviour. There was a significant difference in the average self-reported fluid intake at work between participants that were classified as marginally-adequately hydrated (3120 ± 1574 ml) and optimally hydrated (3959 ± 1286 ml) compared to participants that were dehydrated (1578 ± 526 ml) at the end of the work shift ($p<0.05$). No difference in fluid consumption volume was found between workers that were classified as marginally-adequately hydrated and optimally hydrated at the end of the work shift ($p>0.05$). Participants were categorised into one of the hydration groups based on U_{sg} readings at the end of each day. Fluid intake data was then analysed by hydration group to determine the average fluid consumption from various beverages for each of the classified hydration groups (Table 5c). There was a significant difference in total water consumption between participants that finished the shift in a dehydrated state compared to those that were marginally-adequately hydrated or optimally hydrated ($p<0.05$). No statistical differences were found for the consumption of any of the other reported fluids between the categorised groups ($p>0.05$). There was also no difference in average fluid consumption between workers that rated the intensity of their work shifts as very light-light (2934 ± 1485 ml), moderately hard (3065 ± 1811 ml), or hard-very hard (3500 ± 1036 ml) ($p>0.05$).

Table 5c. Average fluid intake based on beverage type consumed

Hydration Status	Average Fluid Intake (ml) (% of total fluid intake)			
	Beverage Type			
	Water	*Soft Drinks*	*Coffee*	*Tea*
Optimally Hydrated (Day 1 *n* = 8; Day 2 *n* = 6)	3014 ± 1404** (76%)	188 ± 321 (5%)	393 ± 413 (10%)	107 ± 289 (3%)
Marginally-Adequately Hydrated (Day 1 *n* = 5; Day 2 *n* = 5)	2020 ± 1072* (65%)	113 ± 356 (4%)	600 ± 980 (19%)	213 ± 472 (7%)
Dehydrated (Day 1 *n* = 4; Day 2 *n* = 5)	938 ± 753 (59%)	422 ± 422 (27%)	188 ± 177 (12%)	0 ± 0 (0%)

Hydration status based on categories defined as: Dehydrated, U_{sg} > 1.020; Marginally-adequately hydrated, U_{sg} = 1.016 − 1.020; Optimally hydrated, U_{sg} ≤ 1.015. * Significantly different reported intake compared to dehydrated condition (p = 0.042). ** Significantly different reported intake compared to dehydrated condition (p = 0.001). The remainder of fluid not accounted for in this table was from other non-alcoholic drinks including energy drinks, orange juice, sports drinks and milk. Mean values for fluid intake are based on the total *n* value across the two days of data collection.

Alcohol Consumption

A total of six participants (35%) reported consuming alcohol after work on at least one of the days. Four participants consumed alcohol after their shift on day one and six participants reported consuming alcohol after their shift on day two. On average, these participants consumed 4.8 ± 2.9 standard alcoholic drinks (range = 1 – 10).

Subjective Ratings of Body Symptoms

No differences were found between participants who were classified as dehydrated and those classified as marginally-adequately hydrated or optimally hydrated for any of the subjective ratings of body symptoms from the VAS questions (*p*>0.05).

Qualitative Data

Sixteen participants were interviewed. The key response themes relating to each area of enquiry and excerpts from the interviews are outlined below.

Factors affecting Fluid Consumption in the Workplace

Three key themes were identified from this area of enquiry: (1) fluids were readily available at the work site, but this was often only water, (2) the types of fluids available at the work site impeded fluid consumption, and (3) the demands of the workplace negatively affected fluid consumption throughout the day.

The workers generally agreed that there were very few barriers to consuming enough fluid at the workplace. Almost all participants stated that water was freely available at the job site and that fluid availability could not be considered a barrier to inadequate fluid consumption throughout the day. On the other hand, many workers reported that the range of fluids freely available at the worksite were limited (mainly water), and may impact on how much fluid is consumed during the day.

"Water just doesn't cut it sometimes. You can only drink so much water before you end up with a belly ache." (Participant 7, Work site 1)

"We've mentioned this before to work, having Gatorade in the vending machines, but they don't put them in." (Participant 5, Work site 1)

Despite water being freely available to the workers, there was general agreement that the demands of the workplace may impede the workers' ability to consume enough fluid during the day. Many participants stated they found it difficult to leave their work station to reach a water outlet at times, or didn't think about consuming fluid because they were too busy with a task.

"Sometimes the job itself [can be a barrier]. If something goes wrong, it's hard to get from your work station to get some water." (Participant 6, Work site 1)

"You have to walk a bit of a distance, they're [water stations] not really where a lot of primary people are working." (Participant 13, Work site 1)

"If you have water in front of you, you'll drink it. They [the workers] have access to water, but it's just that you're busy doing what you're doing and the next thing you know another hour goes by and you haven't had a drink." (Participant 15, Work site 2)

Attitudes to Alcohol Consumption after Work

Two key themes were identified from this area of enquiry: (1) personal consumption of alcohol after work was perceived as acceptable, and (2) workers who did not drink themselves perceived alcohol consumption by fellow workers to also be acceptable. Most participants reported that drinking alcohol was an individual choice and consuming some alcohol after work was acceptable, provided it didn't influence the worker's ability to perform their job the following day. All participants stated that consuming alcohol after work was acceptable for others, even if they did not do it themselves.

"All the boys work hard enough to kick back and enjoy a beer after work, so I think it's all sweet (sic)." (Participant 14, Work site 2)

"If guys decide to drink after work, well that's their own decision." (Participant 7, work site 1)

"If you drink in moderation, then that's fine. But I don't drink if I'm working hard the next day at all." (Participant 8, Work site 1)

"You can do whatever you like after work. At the end of the day I think we live in a policed society anyway, so you should be able to take responsibility. As long as you're not coming to work under the influence, I have no problem with it." (Participant 16, Work site 2).

Factors Influencing Alcohol Consumption after Work

Several factors were identified as contributing to the consumption of alcohol after work, including: (1) working on a hot day, (2) having a stressful day at work, (3) relaxing after work, (4) attending a social event after work and (5) having alcohol available after work. The most common theme identified as an influential factor for alcohol consumption was the environmental conditions. Almost all workers stated that they were more likely to consume alcohol after a hot day at work.

"If it was a really stinking hot day and I was coming home from work, I might have a beer." (Participant 3, Work site 1)

"Depending on how hot I am. When I finish, sometimes if it's steaming hot. I don't drink beer that often, but sometimes after a hard day and a hot day I'll just go grab a beer because it's just so refreshing." (Participant 16, Work site 2)

The stress of the work day and consuming alcohol as a way to relax was also often reported.

"Just being a hard day, and just wanting to relax. That's what would influence me." (Participant 14, Work site 2)

"Well it's a way to relax after work." (Participant 15, Work site 2)

"If it was a really stressful day, I'd probably have a drink after work. But I suppose it would normally just be on the last shift." (Participant 10, Work site 1)

Other influential factors included having alcohol readily available and attending a social function or event after work.

"If we had a barbeque on the weekend or something and we bought a carton of beer, and there was beer sitting in the fridge, I may well have a beer when I get home from

work. But when there's nothing in the fridge I don't even think about it." (Participant 11,

Work site 1)

"I do thirsty Thursday as a social thing with a mate, and I meet up with some of the

boys at the soccer club on Fridays." (Participant 15, Work site 2)

Awareness of Hydration Prior to Alcohol Consumption

Three common themes were identified from this area of enquiry: (1) workers rarely considered hydration levels before drinking alcohol, (2) if hydration was considered, alcohol was still consumed and (3) workers were more likely to consider hydration levels after drinking alcohol. Most of the participants stated that they didn't think about hydration prior to consuming alcohol.

"No, it [hydration] wouldn't enter my mind to be quite honest." (Participant 3, Work site

1)

"I wouldn't say I sat down and thought about it [hydration]...... It's really something

I really think about when I'm having a drink. I'm not sitting there thinking oh gee I hope

I'm not dehydrated. To me I'm replenishing myself." (Participant 5, Work site 1)

The few participants who did report that they think about hydration also stated that it wouldn't stop them from having an alcoholic drink.

"Occasionally [I would consider my hydration], but I wouldn't be like oh I better not

have a drink because I'm dehydrated." (Participant 16, Work site 2)

However, many of the participants did state that they thought about hydration levels after consuming alcohol.

"I haven't thought about it before, but I do think about it afterwards. Before I finish up or go to bed, I'll make sure that I start drinking some water. I normally start to think about it a couple of hours before I'm about to go to bed." (Participant 13, Work site 1)

Only one participant mentioned that they would consider their hydration status before drinking alcohol and also take some action to rectify possible dehydration before consuming alcohol.

"Yeah I do think about it [hydration status before drinking alcohol]. But I still have a drink anyway. Sometimes if I think I'm really dehydrated, I'll have a glass of water, and then have a beer. If I feel dehydrated I certainly won't go straight into having a beer." (Participant 9, Work site 1)

5.5 Discussion

The purpose of the study was to determine the hydration status of industrial workers, and explore the attitudes, perceptions and practices of individuals toward post-work rehydration and alcohol consumption. Urine specific gravity recordings from this group of workers showed that almost a third (n = 22/68, 32%) of the urine samples collected had U_{sg} readings indicating some degree of dehydration. Most of these were from recordings taken at the beginning of the work shift. These findings indicate a lower proportion of dehydrated workers compared to previous Australian studies (Brake & Bates, 2003; Carter et al., 2006; Miller & Bates, 2007; Hunt et al., 2011). However, this may be due to differences in occupational conditions between the studies such as the intensity of manual tasks performed by the workers and more extreme work environments. Nevertheless, the current observations indicate that even under less extreme environmental conditions, many industrial workers are likely to experience fluid loss that results in dehydration. Given the number of workers in these types of occupational environments, there is a

high risk of workers developing heat-related illness and for dehydration-related accidents and injuries to occur.

Although not all of the participants in this study consumed alcohol, the opinion of workers that alcohol consumption after work is acceptable was widespread. Interestingly, the perceptions of workers toward alcohol consumption after work reflected the quantitative data. Every participant that consumed alcohol also stated that drinking alcohol after work was acceptable. Those that didn't consume alcohol generally reported that they didn't do it themselves, but that it was acceptable for others to, provided that it was not excessive. These findings reflect the popular subculture of industrial occupational groups toward alcohol consumption, which has been described in previous studies as being part of a valued and leisure-time male oriented culture (Janes & Ames, 1989; Berry et al., 2007). Overcoming the workplace culture and workers' perceptions toward alcohol consumption may pose one of the greatest challenges in promoting effective rehydration strategies and workers' overall health and safety. Further research is required in order to develop a better and more precise understanding of the role work plays in the way people consume alcohol. This may assist with the development of strategies that can be used to change workers' values toward alcohol consumption.

Participants in the present study reported several influential factors for alcohol consumption after work. Two common themes were the consumption of alcohol in order to relax or relieve stress after work and for social or celebratory reasons. These factors have been emphasised in previous studies (Farber et al., 1980; Abbey et al., 1993), and suggest that alcohol use is associated with both the alleviation of undesirable states and as a means to obtain particular social goals (Farber et al., 1980; Abbey et al., 1993). However, of particular importance in the context of the current study was the number of workers that stated they would be more likely to consume alcohol after work in hot conditions. Stressful work situations including conditions related to the physical work environment (hot or cold environments) have been suggested by others as a cause

145

of employee alcohol use (Frone, 1999). In extreme hot or humid conditions, there is potential for greater fluid loss and increased opportunity for dehydration to occur. If industrial workers are more likely to consume alcohol under extreme environmental conditions, then it is important that they take an active approach to managing their hydration status.

The consumption of alcohol under conditions of mild or moderate dehydration may have direct implications for workers. Dehydration may impact the pharmacokinetic response to alcohol and increase the likelihood of engaging in risk-taking behaviour such as drink-driving. One could also easily speculate that the combined effects of alcohol and dehydration are likely to exacerbate cognitive impairment rather than be complementary in nature. This could have serious consequences for individuals who consume alcohol after finishing work in a dehydrated state and then consider driving. The findings from this study suggest that hydration was not a factor influencing the likelihood of consuming alcohol after work. Together with the perceptions toward post-work alcohol consumption, the importance of developing appropriate messages that reflect the implications of alcohol consumption by individuals likely to experience dehydration at the work site is clear. There is a need to establish and maintain a culture of hydration awareness at industrial work sites (Miller & Bates, 2010). Strategies must be incorporated that encourage good hydration behaviour to reduce the likelihood that individuals will consume alcohol in a dehydrated state. From a worker's perspective, this requires a conscious decision to monitor hydration status and act appropriately to remain hydrated both prior to starting work and throughout the work day (Markovsky, 2010). Employers also play an important role and must ensure that education on hydration and the implications of alcohol consumption are an ongoing part of employee communications (Markovsky, 2010).

Fluid was readily available at the work sites in this study and participants generally agreed that there were few barriers to consuming enough fluid at the workplace. However, the appeal of beverages available for consumption and the demands of the workplace were identified as

possible impediments to adequate rehydration. A critical component of avoiding dehydration in the workplace is ensuring that fluid is readily accessible and appealing to the workers (Markovsky, 2010). There is some evidence suggesting that carbohydrate-electrolyte beverages are beneficial for rehydration in working environments because they are highly palatable and promote increased fluid consumption (Clapp et al., 1999; Clapp et al., 2000). However, other evidence suggests that hydration can be adequately maintained if water is provided at regular intervals during the work day (Clapp et al., 2002). The availability of fluids in the workplace may also influence post-work beverage choice, particularly when options are limited at the work site and workers are accustomed to a wide variety of beverages of their preference outside the occupational setting (Clapp et al., 2002). A number of studies have shown that the palatability and flavour appeal of fluids consumed in the workplace decreases from pre- to post- shift (Clapp et al., 1999; Clapp et al., 2000). This may also help explain why some individuals consume alcoholic beverages after work. Further investigation into the effects of workplace beverage availability on post-work beverage choice and alcohol consumption is required.

A potential limitation of this current work is the selection bias of participants involved in the study. The researchers had to be particularly attentive to the demands of the worksite to ensure minimal disruption to the work activities of participants. As such, many of the workers who performed extremely demanding tasks and were most likely to experience the greatest levels of dehydration were not available to participate in the study. In addition, there were difficulties in the recruitment and retention of participants, as many of the workers were sceptical about providing urine samples for analysis of hydration status. These issues have also been reported in previous studies (Cook et al., 2004). It is likely that participants with some interest in health and hydration are over-represented in this study. Participants were aware that hydration assessment was being measured in the study, which may have had an influence on drinking behaviour over the data collection period. Thus, dehydration and post-work alcohol consumption may be more

147

common in these occupational groups than presented here. Furthermore, self-reported methods are likely to result in underestimation of alcohol consumption (London, 2000). In addition, data was collected from participants on the final two day shifts of their work roster, which varied between individuals, but was most often a mid-week day. It is likely that alcohol consumption would be greater on a Friday or weekend shift compared to a mid-week shift. Thus, the degree to which post-work alcohol consumption occurred may well be underestimated in this study. Finally, this study involved a small convenience sample of male industrial workers from two types of industries. As such, these findings may not be representative of the broader industrial workforce. Future research should examine fluid balance and associated alcohol consumption parameters across a larger range of industrial work sites and gender groups. Understanding these behaviours is critical to addressing issues associated with dehydration within the workplace. It is also important to acknowledge that the results of this study are largely descriptive and exploratory in nature rather than specifically testing a hypothesis. As such, further research involving larger samples, targeting specific hypotheses may be warranted in the future.

In summary, the hydration status of industrial workers was monitored over two consecutive days at work, prior to exploring the workers' attitudes, perceptions and practices toward alcohol consumption. A high proportion of workers were inadequately hydrated, both at the beginning and end of their shifts over the data collection period. The majority of workers believed it was acceptable to consume alcohol after work and indicated a lack of consideration for hydration levels prior to consuming alcohol. Several of the participants in this study (across a range of hydration levels) participated in alcohol consumption. These results indicate that industrial workers may be particularly vulnerable to dehydration and participate in post-work rehydration practices that include the consumption of alcohol. The consumption of alcohol under conditions of dehydration may have direct implications for workers. Further research is required in order to gain a better understanding of hydration in the workplace and workers' attitudes and behaviours

toward post-shift fluid consumption (including alcohol). This may assist with the development of appropriate public health campaigns highlighting the implications of alcohol consumption in situations where dehydration is anticipated.

Chapter Six: Research Study Two - Alcohol Pharmacokinetics and Risk-Taking Behaviour Following Exercise-Induced Dehydration

Reader's Note:

The information in this section has been published as an original research paper:

Irwin C, Goodwin A, Leveritt M, Davey AK, Desbrow B. Alcohol Pharmacokinetics and Risk-Taking Behaviour Following Exercise-Induced Dehydration. *Pharmacology Biochemistry and Behavior*, 2012; 101(4): p609-616.

The co-authors of this publication confirm that the research candidate has made the following contributions to this study:

- Developed the study design.

- Completed the human research ethics application.

- Supervised and assisted with data collection.

- Conducted analysis of the data.

- Prepared manuscript for submission to journal.

- Presented research at a national and international conference.

Signed: _____   **Date: 06/09/13**

Signed: _____   **Date: 06/09/13**

Signed: _____   **Date: 06/09/13**

Signed: _____   **Date: 06/09/13**

6.1 Abstract

Aim: This study investigated the influence of exercise-induced dehydration on alcohol pharmacokinetics, subjective ratings of impairment, and risk-taking behaviours. **Methods:** Twelve male volunteers participated in three experimental trials completed in a randomised cross over design separated by at least seven days. In one trial, participants exercised to cause dehydration of ~2.5% body weight loss. For the other trials, participants were required to be in a rested and euhydrated state. A set volume of alcohol was then consumed in each trial and participants were monitored over a four hour period. Blood and breath alcohol samples were collected throughout and analysed to calculate pharmacokinetic variables associated with the blood alcohol curve. Total urine production, estimates of BrAC, and subjective ratings of intoxication and impairment were also recorded throughout each trial. **Results:** No difference was found in the pharmacokinetics of alcohol between any of the trial conditions. BrACs were higher than BACs for two hours following alcohol consumption, but lower at measures taken three and four hours post ingestion. Participants' ratings of confusion and intoxication were significantly lower, and they were more willing to drive in the dehydration trial compared with one of the euhydration trials. **Conclusions:** These findings suggest that dehydration or other physiological changes associated with exercise may have an ability to influence the subjective effects of alcohol and increase the likelihood of risk-taking behaviours such as drink-driving. However, further research is required to examine the effects of alcohol under conditions of exercise-induced fluid loss in order to clarify these findings.

6.2 Introduction

It is well established that acute alcohol consumption influences individual behaviour and can significantly impair performance on a range of complex tasks such as driving a motor vehicle (Mitchell, 1985). The consumption of alcohol increases the risk of motorists being involved in a crash (Blomberg et al., 2005). For this reason, statutory alcohol driving limits are enforced as a means of reducing alcohol-impaired driving. In many countries driving with a BAC above 0.05% is considered illegal. Despite extensive public health campaigns reinforcing the risks associated with drink driving, research indicates that a considerable proportion of drivers have concentrations of alcohol in their blood that impair their road use skills (World Health Organisation, 2007). One of the major issues in having a statutory driving limit above zero is that individuals estimate their BAC based on alcohol consumption and justify their actions to operate a motor vehicle if they predict a level below the legal driving limit. This is particularly concerning, given that individual responses to alcohol ingestion are widely variable (O'Neill et al., 1983).

The fate of alcohol in the human body after ingestion has been well documented (Eckardt et al., 1998). Alcohol ingestion results in an increase in BAC, after which it reaches a peak level before being eliminated from the body. The general behaviour of BAC over time follows what is known as

the blood alcohol curve (Pikaar et al., 1988). Typical analysis of the curve allows for determination of variables describing the absorption and elimination kinetics of alcohol, including peak BAC (C_{max}), time to reach peak BAC (t_{max}), area under the blood alcohol curve (AUC), the volume of alcohol distribution (V_d), the half-life of alcohol ($t_{1/2}$), clearance (Cl), and the mean residence time (MRT).

However, alcohol absorption and elimination vary considerably amongst individuals, and the pharmacokinetics of alcohol is subject to influences from a variety of factors. These include individual characteristics such as age (Lucey et al., 1999), gender (Baraona et al., 2001), genetics (Whitfield, 1994) and body composition (Marshall et al., 1983) as well as alcohol administration variables such as alcohol dose (O'Neill et al., 1983), concentration (Roberts & Robinson, 2007), type of alcoholic beverage (Roine et al., 1993), the consumption and composition of meals (Ramchandani, Kwo, et al., 2001), the timing of alcohol consumption (O'Neill et al., 1983) and individual patterns of alcohol exposure (Whitfield & Martin, 1994).

The individual characteristics described are considered to influence the proportion of water in the body and have been thought to make significant differences in peak BACs attained following alcohol ingestion (O'Neill et al., 1983). The distribution of alcohol throughout the body is largely governed by the water content of tissues and organs (Eckardt et al., 1998), with the volume of distribution of alcohol comparable to total body water (Ramchandani, Bosron, et al., 2001). A reduction in total body water content is expected to decrease the dilution of alcohol (Pohorecky & Brick, 1988), which could consequently result in an increased BAC and a change in other pharmacokinetic variables associated with the normal alcohol response (Roberts & Robinson, 2007).

Changes in the pharmacokinetic profile of alcohol are important to consider given that the associated symptoms and subjective effects of alcohol are directly related to BAC (Ekman et al., 1963; Nicholson et al., 1992). A change in alcohol pharmacokinetics could impact on actual levels

of impairment experienced and may result in changes to perceived intoxication levels, which could have direct implications for individuals who operate machinery or drive a motor vehicle following alcohol consumption. Therefore, it is important to consider from both an individual and population health perspective all factors that may influence alcohol pharmacokinetics including changes in TBW content.

The relationship between alcohol and TBW content suggests that hydration level may influence BAC (Thompson, 1997). Hydration level is acutely variable in individuals (Shirreffs, 2009) and many people consume alcohol after a period of physical activity or exertion that results in fluid loss through sweating (e.g. after a sporting match or hard physical labour). The consumption of alcohol under conditions of mild or moderate dehydration may result in changes to alcohol's pharmacokinetic profile compared to conditions where fluid deficit is not present.

The influence of fluid loss through sweating on alcohol pharmacokinetics and subjective ratings of alcohol-related impairment is yet to be investigated. Therefore, the aim of this study was to investigate whether dehydration induced through physical exercise influences the blood and breath responses to a moderate amount of ingested alcohol and alters the subjective ratings of alcohol's effects to a greater extent than the daily intra-individual variability observed without an acute fluid change. It was hypothesised that alcohol pharmacokinetic variables associated with the blood alcohol curve would be significantly affected by dehydration, leading to higher BAC levels when participants were dehydrated and greater ratings of the perceived intoxication effects of alcohol compared to those observed during euhydrated trials.

6.3 Materials and Methods

The participant group, experimental design, pre-experimental procedures and experimental procedures for this study have been outlined in detail in Pilot Study Two (Chapter 4.3). In addition

to the experimental procedures described in Pilot Study Two, the following procedures exclusive to this investigation were included:

1. Tympanic temperature (T_t) measurements were collected (Braun ThermoScan®, Welch Allyn Inc., San Diego, CA, USA) prior to exercise and following the rest period.

2. Following consumption of the beverage participants completed a questionnaire rating the subjective effects of alcohol using a computerised VAS (Marsh-Richard et al., 2009).

Breath alcohol concentrations

Breath alcohol concentrations were analysed using the Alcolizer LE breathalyser (Alcolizer Pty Ltd), as described in Pilot Study Two (Chapter 4.3).

Subjective ratings questionnaire

The questionnaire consisted of 10 statements relating to subjective estimates of mood, bodily symptoms, intoxication and alcohol-induced impairment. For six of the scales, participants were presented with a 100mm line, the ends of which were marked with antonyms (nauseated-not nauseated, happy-sad, tense-relaxed, alert-drowsy, confused-clearheaded, well coordinated-clumsy), and they adjusted the position of a cursor on each line using a mouse to indicate how they felt at that moment. The score was taken as the cursor position based on percentage of scale length. These scales were adapted from those that have been used in previous research (Bond & Lader, 1974). For the remaining four scales participants rated subjective intoxication and impairment using 100 mm visual-analogue scales in a similar manner. Ratings were obtained on a scale between 0mm 'not at all' and 100mm 'very much' in response to the questions "how able are you to concentrate", "how intoxicated do you feel", "how willing would you be to drive a car", and "how willing would you be to drive a car less than 5km". Similar scales have been used in

other studies of alcohol and driving and are sensitive to the effects of the drug (Fillmore, 2001; Harrison et al., 2007; Fillmore et al., 2008).

Assay of ethanol and pharmacokinetic analysis

Plasma sample procedures and subsequent ethanol analysis are detailed in Pilot Study Two (Chapter 4.3). In addition to these procedures, individual pharmacokinetic parameters were estimated using WinNonlin® Standard Edition Version 6.2 (Pharsight Corporation, Mountain View, CA, USA) employing a non-compartmental model. The area under the time curve from time zero to 240 min (AUC0-240) was calculated using the linear trapezoidal rule.

Statistical analysis

All statistical procedures were performed using SPSS for Windows, Version 19.0 (SPSS Inc., Chicago, IL, USA). Statistical analysis of alcohol pharmacokinetic variables (C_{max}, t_{max}, AUC, V_d, and $t_{1/2}$) and differences between BAC and BrAC measures at each time point were conducted using one-way repeated-measures ANOVA. Pairwise comparisons (LSD) were performed where significant main effects were present. Coefficients of variation (CV) for BAC and BrAC across the two euhydration trials were calculated by standard methods. All additional analyses of blood and breath alcohol concentration and scores derived from the VAS questionnaires were subjected to a two-way ANOVA; Protocol (DA, A1, A2) x Time (min), with both as repeated measures factors. Several studies have supported the use of parametric methods, particularly ANOVA as an appropriate technique to compare VAS measurements among groups (Maxwell, 1978; Philip, 1990; Wewers & Lowe, 1990; Dexter & Chestnut, 1995; Ahearn, 1997). Post hoc analysis (LSD) was performed on all significant *F* ratios ($p<0.05$). Statistical significance was accepted at $p<0.05$. All data are reported as mean±standard deviation unless otherwise specified.

6.4 Results

Body mass

Participants began each of the trials in a hydrated state. There was no difference in U_{sg} measurements recorded between trials (1.007±0.007, 1.010±0.005 and 1.008±0.007 for trials A1, A2 and DA respectively, *p*>0.05). All participants underwent the dehydration protocol and were successful in achieving similar levels of hypohydration. The mean body weight loss in the DA trial was equal to 2.0±0.3 kg (range 1.3-2.3 kg). This was equivalent to 2.5±0.3% of initial body weight (range 1.8-3.0%). The estimated mean TBW content of the participants was 45.7±2.4 litres (range 41.2-49.8 litres) which was equivalent to 59.3±2.3% (range 55.3-63.0%) of the total measured body weight. Using these values, mean TBW loss was calculated as 4.3±0.4% (range 2.9-5.1%). The mean duration of exercise to achieve the required dehydration level was 86±18 min (range 60-120 min).

Alcohol consumption

The mean volume of alcohol consumed was 114±6ml of vodka, which was equivalent to providing participants with 0.44±0.02 g/kg BW of alcohol or 3.4±0.2 standard alcoholic drinks. The mean total volume of the beverage including the vodka and juice was equal to 342±18ml. All participants consumed the beverage within the 10 min time allocation with no complications or tolerance related issues reported.

Urine volume and fluid balance

Urine output was measured at the end of each hour during the four hour monitoring period. The total urine volumes produced over the four hours for each trial are shown in Fig. 6a. A significantly greater volume of urine was excreted in the euhydration trials compared to the dehydration trial (1234±421ml and 1130±373ml vs. 300±125ml for trials A1, A2 and DA

respectively, *p*<0.05). The intra-individual variability in total urine production across the two euhydration trials was CV = 19%. Peak urine output occurred 60 min post alcohol ingestion on all trials, with significantly higher volumes recorded during the euhydration trials compared to the dehydration trial at 60 min and 120 min post alcohol consumption (*p*<0.05). Calculation of whole body net fluid balance for each trial was performed using estimated sweat loss, fluid consumption and the volume of urine produced (Fig. 6b). Under all experimental conditions, participants completed the trial in a state of negative fluid balance (-892±421ml, -787±368ml, -1908±331ml for trials A1, A2, and DA respectively). Whole body net fluid balance was significantly lower throughout the dehydration trial compared to the euhydration trials (*p*<0.05).
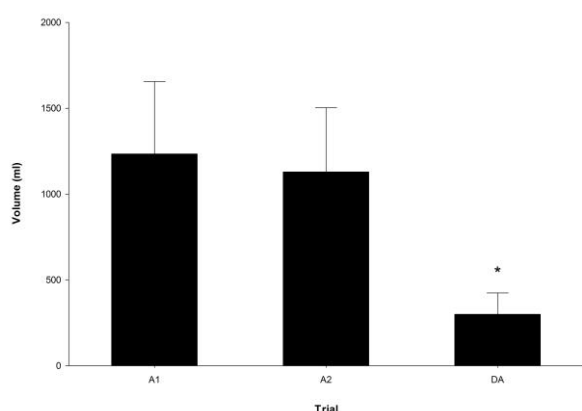

Fig. 6a. Total cumulative urine volume produced over the four hour monitoring period post alcohol ingestion on each trial. * Significant difference in volume compared to other trials. A1, euhydration and alcohol trial one; A2, euhydration and alcohol trial two; DA, dehydration and alcohol trial.
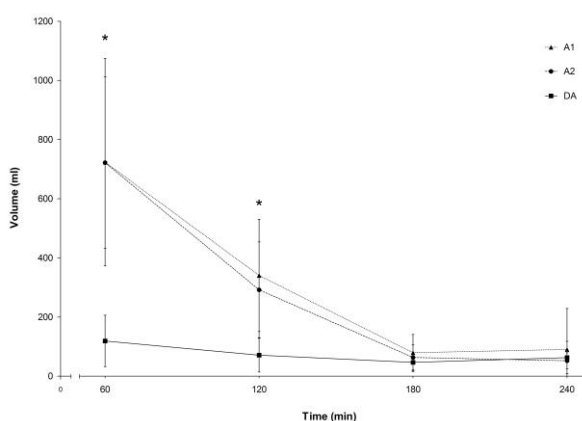
Fig. 6b. Urine volume produced at each hour of the monitoring period. *Significant difference in volume of urine produced for the A1 and A2 trials compared to the DA trial. A1, euhydration and alcohol trial one; A2, euhydration and alcohol trial two; DA, dehydration and alcohol trial.

Blood and breath alcohol concentrations

The mean concentrations of alcohol measured in blood and breath samples for each of the three trials are shown in Fig. 6c. There were no differences in BAC or differences in BrAC between the three trials at any of the measured time points, $F_{(2,22)}=0.541$; *p*=0.590. In all of the trials BrACs were higher than BACs over the first two hours following alcohol consumption. For the final two hours of monitoring, BACs were higher in all trials compared to BrAC measures. Peak BrACs

were achieved 15-30 min post alcohol ingestion with mean levels of 0.069±0.014%, 0.072±0.018%, and 0.070±0.011% recorded for the A1, A2 and DA trials respectively. Peak BACs were achieved between 30 and 45 min post alcohol consumption.
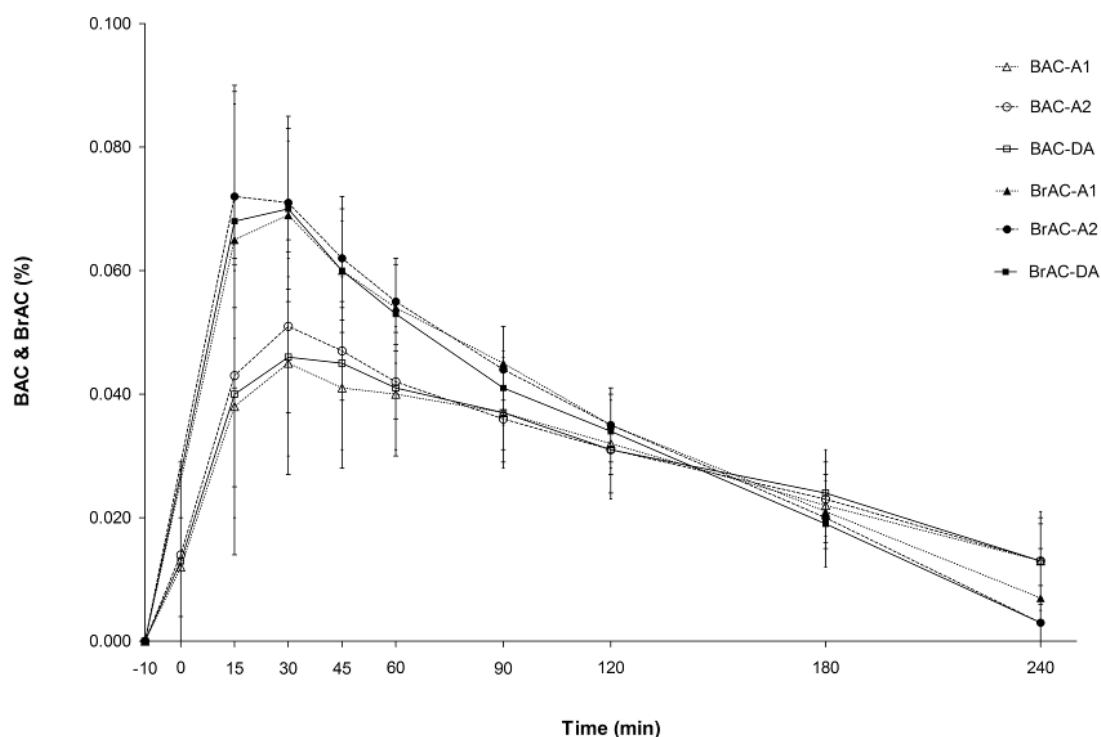

Fig. 6c. Blood and breath alcohol concentrations recorded at each time point over the four hour monitoring period. A1, euhydration and alcohol trial one; A2, euhydration and alcohol trial two; DA, dehydration and alcohol trial.

Mean peak BAC values and data from the pharmacokinetic analysis for each trial are shown in Table 6. There was no significant difference in any of the pharmacokinetic parameters between trials ($p>0.05$). Variability in BrAC measures was determined by comparing the duplicate samples collected within trials. The inter-trial variability was similar across all trial conditions (CV = 2.5%), indicating that the breathalyser instrument was sensitive enough to detect changes in BrAC across the different trial conditions. The degree of variability in individuals' BrAC and BAC responses across trials was determined by calculating the CVs for both variables across the two euhydration

trial conditions (trials A1 and A2). A high degree of intra-individual variability was evident across trials for these measures, with CVs of 14% and 23% for BrAC and BAC responses respectively.

Table 6. Pharmacokinetic data following the consumption of alcohol in each of the trial conditions (*n*=12)

Parameter	Trial		
	A1	**A2**	**DA**
C_{max} (g.dl^{-1}) (CV%)	0.050±0.018 (36%)	0.055±0.015 (27%)	0.053±0.015 (28%)
t_{max} (min) (range)	40.00±21.53 (15-90)	35.00±13.31 (15-60)	41.25±15.83 (15-60)
AUC_{last} (g.dl^{-1}h) (CV%)	1.19±0.30 (25%)	1.23±0.20 (16%)	1.22±0.32 (26%)
$t_{1/2}$ (h) (range)	1.89±1.30 (0.58-5.69)	1.72±0.62 (0.89-3.24)	2.06±1.69 (0.92-7.21)
V_d (l)	49.07±18.39	46.29±7.77	49.47±16.67
Cl (l.h^{-1})	21.01±7.88	20.11±5.14	20.44±7.27
MRT_{last} (h)	1.69±0.22	1.63±0.13	1.67±0.17

C_{max} – maximum concentration, t_{max} – time to maximum concentration, AUC_{last} – area under the alcohol curve calculated to the last time point measured, $t_{1/2}$ – half life, V_d – volume of distribution assuming bioavailability, Cl – clearance rate, MRT_{last} – mean residence time calculated to the last time point measured), CV% - coefficient of variation (SD/mean x 100), Values are mean±SD.

Breath alcohol concentration estimations

Participants' predictions of BrAC are shown in Fig. 6d along with the actual BrAC measures recorded. While there was a slight tendency for participants to predict lower values during the euhydration trial (A1) and the dehydration trial (DA) compared to the actual BrAC measures on these trials, the variability in subjective predictions of BrAC resulted in no significant difference between actual measures and the estimations at any time point across all of the trials [$F(1,11)$=0.921 for trial A1, $F(1,11)$=0.001 for trial A2, and $F(1,11)$=1.78 for trial DA; *Ps*>0.05]. There was also no difference in the predictions of BrAC between the three trials [$F(2,22)$=2.226;

p=0.132], with participants able to estimate BrAC with some degree of accuracy, regardless of trial conditions.
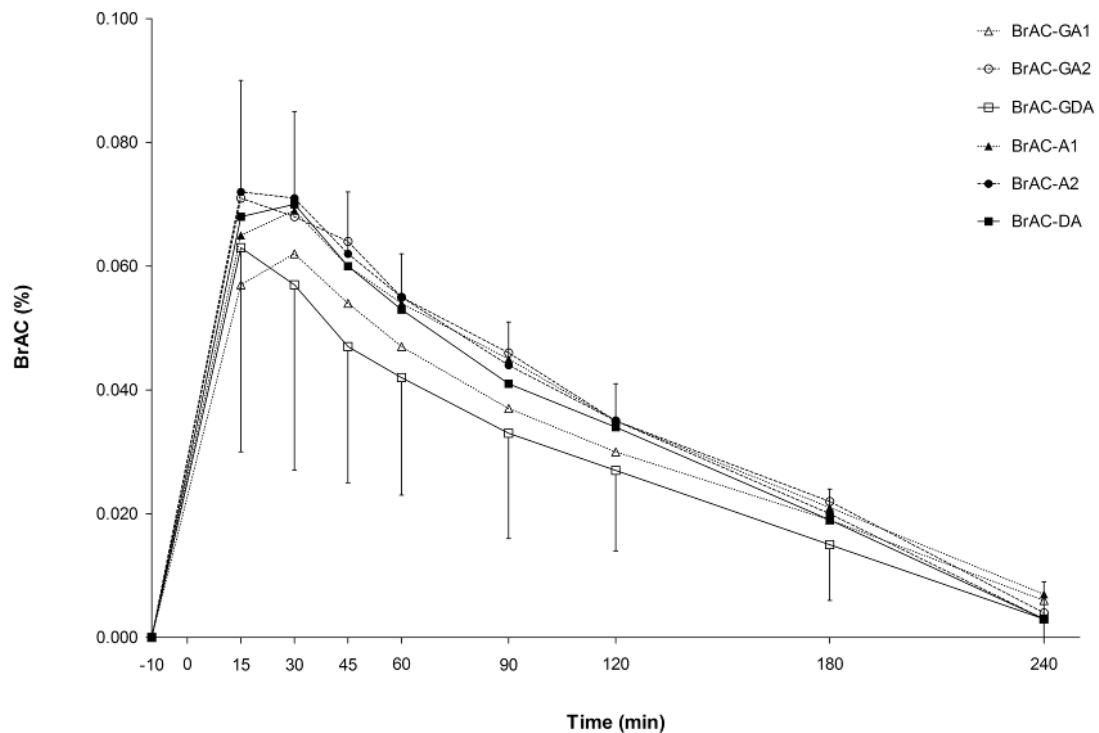

Fig. 6d. Breath alcohol concentrations and participant predictions of BrAC recorded at each time point over the four hour monitoring period. A1, euhydration and alcohol trial one; A2, euhydration and alcohol trial two; DA, dehydration and alcohol trial; G, participant guess. Error bars have been removed on some data points to provide clarity.
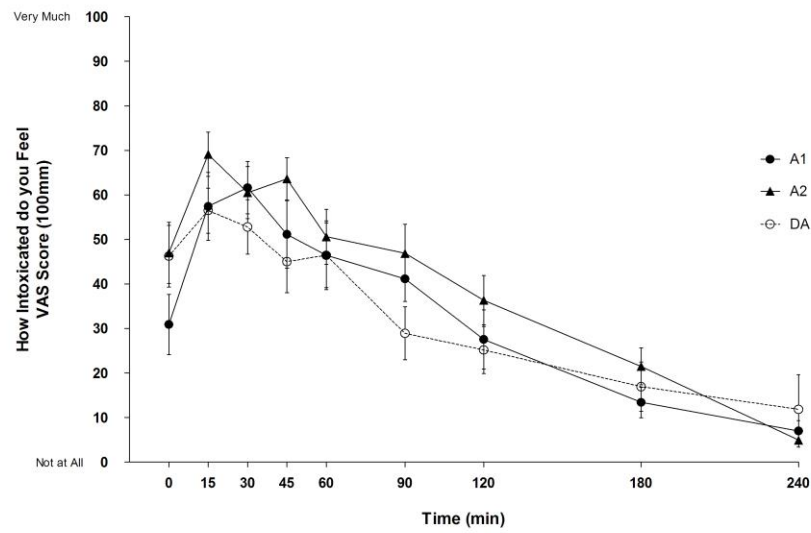
Subjective ratings

A number of significant effects were found on measures derived from the VAS questionnaires (Fig. 6e). On the confused-clear headed scale there was a significant main effect for protocol, $F_{(2,22)}=4.05$; *p*=0.032, and time $F_{(8,88)}=7.82$; *p*<0.01, but no protocol x time interaction, $F_{(16,176)}=0.780$, *p*=0.707. Post hoc analysis revealed higher ratings of confusion in the A2 trial compared to the DA trial from 15 min post alcohol consumption (*p*<0.05). In response to the question "how intoxicated do you feel", there was a main effect for protocol, $F_{(2,22)}=3.65$; *p*=0.043, and time, $F_{(8,88)}=34.33$; *p*<0.01, but no protocol x time interaction, $F_{(16,176)}=1.03$; *p*=0.433. Ratings of intoxication increased over the first 15 min in all trials and then decreased thereafter. Participants' ratings of intoxication were significantly higher in the A2 trial compared to

the DA trial ($p<0.05$). A significant main effect for protocol, $F_{(2,22)}=3.89$; $p=0.036$, and time, $F_{(8,88)}=8.27$; $p<0.01$, were also found for responses to the question "how willing would you be to drive a car less than 5km", with no protocol x time interaction, $F_{(16,176)}=0.27$; $p=0.998$. Participants were more likely to drive in the DA trial compared to the A2 trial ($p<0.05$). No main effects of protocol or protocol x time interaction were found on any of the other subjective variables. However, a main effect of time was present for the nauseated-not nauseated, well coordinated-clumsy, ability to concentrate, and willingness to drive a car scales ($ps<0.05$). Participants felt less nauseous, less clumsy, were more able to concentrate and were more willing to drive a car as each trial progressed. There were no main effects of time for the alert-drowsy, happy-sad, and tense-relaxed subjective scales ($ps>0.05$).
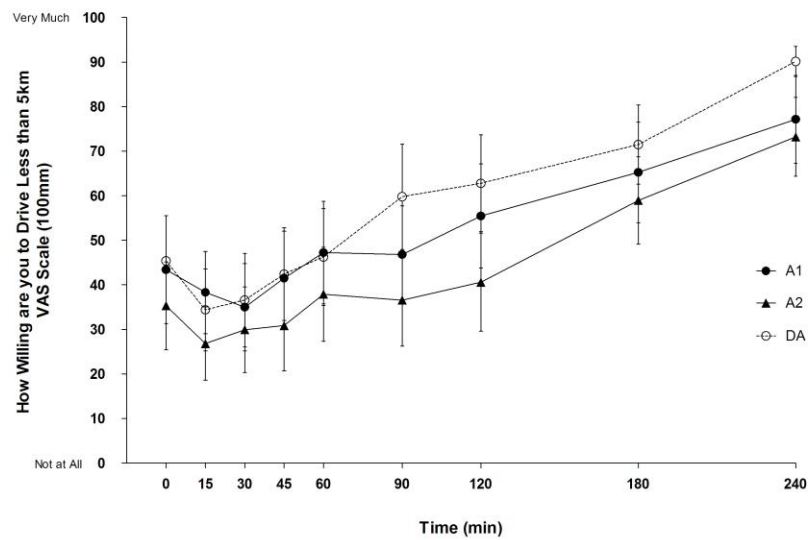
(i)
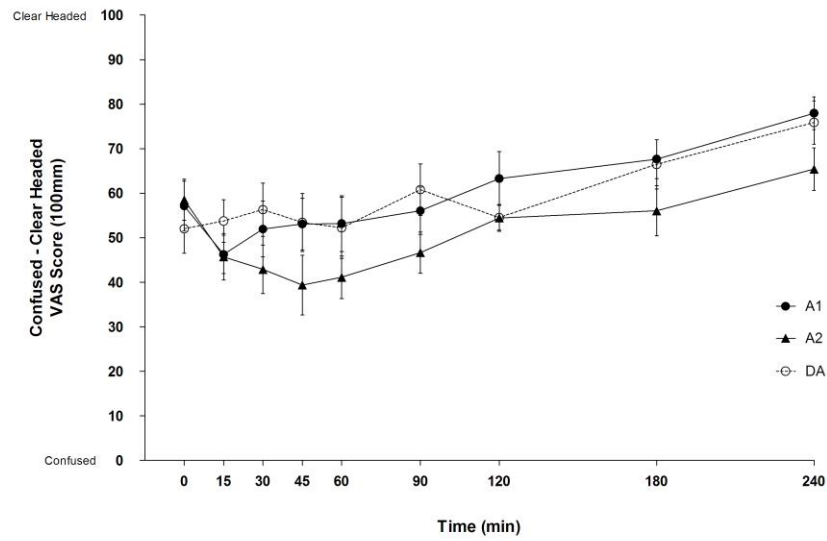
(ii)

(iii)

Fig. 6e. Subjective ratings from visual analogue scales. (i) confused - clear-headed scale. (ii) how intoxicated do you feel scale. (iii) how willing would you be to drive less than 5km scale. A1, euhydration and alcohol trial one; A2, euhydration and alcohol trial two; DA, dehydration and alcohol trial. Values are mean±SEM.

6.5 Discussion

In this study the effect of dehydration, induced by physical exercise, on blood and breath alcohol pharmacokinetics and risk-taking type behaviour was investigated. Contrary to our hypothesis, no differences were observed in peak BrAC and peak BAC between the different trial conditions. Additionally, there were no differences in any of the other pharmacokinetic variables measured including AUC, t_{max}, $t_{1/2}$, V_d, Cl, and MRT as a result of the dehydration condition. These results suggest that acute changes in total body water content as a result of exercise induced sweat loss have no impact on alcohol pharmacokinetics when a moderate dose of alcohol is consumed.

The lack of observed differences in pharmacokinetic response between the different trial conditions was evident regardless of whether fluid loss was considered as changes in body weight or estimated total body water loss. One possible explanation for this may be that the diuresis due to alcohol was much greater in euhydrated subjects, particularly in the first 60 min following alcohol ingestion (~720ml for the euhydrated trials and ~120ml for the dehydrated trial). Prior to consumption of the alcoholic beverage, a difference of ~1950ml in net fluid balance existed between the euhydration and dehydration trials. The total water loss through urine (average of ~840ml for the two euhydration trials), while not as large as that lost though sweat during the exercise, is substantial enough to reduce the difference in hydration status between the participants in different arms of the trial.

Other factors are also known to influence alcohol absorption and elimination, such as body composition (i.e. fat distribution). Higher peak BACs are typically seen in older males compared with their younger counterparts (Davies & Bowen, 1999) and this is often explained by differences in body composition that occur with ageing (Vestal et al., 1977). Participants in this study were comparable in age and body size, however measures of body composition (percent body fat) were not collected. Whilst alcohol doses were administered according to estimates of individual total

163

body water content (Watson et al., 1981), it is possible that subtle differences in body composition (percentage of body fat) between individuals may be responsible for the large variation observed in BAC and BrAC, resulting in no differences between trial conditions. However, this study did employ a cross-over deign protocol and whilst this would not have eliminated between subject variables, participants acted as their own control, reducing the influence of confounding co-variates.

Genetic differences in alcohol metabolising enzymes may also influence the pharmacokinetics of alcohol (Crabbe et al., 1999; Li et al., 2001; Ramchandani, Bosron, et al., 2001; Schuckit et al., 2004). The between-individual variation in alcohol pharmacokinetics has been associated, in part due to allelic variants of the genes encoding the alcohol metabolising enzymes, alcohol dehydrogenase and aldehyde dehydrogenase (Ramchandani, Bosron, et al., 2001). Whilst gender and ethnicity were accounted for in this study, this does not control for the prevalence of genetic polymorphisms that may exist in individuals, which may also help to explain the variance in pharmacokinetic responses observed. Further investigation of the factors regulating alcohol pharmacokinetics in a variety of hydration conditions is required.

In general, the results obtained from blood and breath analysis showed similar trends. However, higher alcohol concentrations were recorded when measured by breath analysis during the first two hours post consumption compared to blood alcohol analysis. Conversely, BrACs were lower than BACs from three hours post alcohol ingestion. These results are consistent with previous research that identified higher C_{max} values measured by breath analysis compared to blood analysis (Pikaar et al., 1988), and may reflect the difference between arterial blood alcohol levels measured at the lung and venous blood alcohol levels derived from the blood samples. The concentrations in arterial and venous blood are equal approximately 60-120 min after the end of drinking (Jones, 2010). Prior to this, concentrations in the arterial blood are higher than in the

venous blood, and at later times the concentration of alcohol in venous blood is slightly higher than in arterial blood (Jones, 2010).

Another possible explanation for the non-significant findings in pharmacokinetic variables reported may be due to the large intra-individual variability in alcohol levels, inducing a type II error, whereby we were unable to detect subtle changes in the pharmacokinetic response. Several other studies have also reported large variability in the pharmacokinetics of alcohol (CVs up to 20%), both between and within individuals (Schønheyder et al., 1942; Jones, 1984; Jones & Jönsson, 1994; Yelland et al., 2008). The methods used to evaluate alcohol response in this study are typical of those used in other studies examining the effects of alcohol. More importantly, however, these methods are reflective of those used in the field by law enforcement officers to determine the intoxication levels of motorists on the road. Despite our original hypothesis, it is apparent that alcohol levels under conditions of exercise induced dehydration to 2.5% BW loss are not different to those that would be expected as a result of this normal intra-individual variability. As such, individuals who consume alcohol following an acute period of fluid loss through sweating are no more at risk of being detected over the drink driving limit than they would be otherwise.

Of greater concern, however, is the possibility that their judgement about whether or not to drive may be affected. Further research is required to clarify these findings. Given the intra-individual variability in alcohol response reported in this study, it may be more appropriate to investigate the effects of dehydration on alcohol pharmacokinetics and the associated subjective responses using the alcohol clamping technique described in other studies (O'Connor et al., 1998; Ramchandani & O'Connor, 2006). Whilst not reflective of actual drinking practices, these methods have been shown to reduce experimental variance and may provide more meaningful comparisons between different trial conditions.

Interestingly in this study, participants' subjective ratings of confusion and feelings of intoxication were lower during the dehydration trial. However, these results were only significant

165

in comparison to the second euhydration trial (A2) and no differences were observed between trials A1 and A2 or A1 and DA. There was a large degree of variability in individual predictions of BrAC, particularly when actual BACs were higher, suggesting that acute alcohol consumption clearly results in poor early estimations of intoxication level or a reduced level of concern in predicting the BrAC level. There was a tendency for BrAC predictions to be lower during the DA trials, which may explain why ratings of confusion and intoxication were lower during these trials compared to the A2 trial and also why participants were more willing to drive a motor vehicle a short distance under these conditions.

There is some evidence that physical exercise can facilitate cognitive function, which is often explained through a positive effect of increased arousal levels (Hogervorst et al., 1996; Etnier et al., 1997; Collardeau et al., 2001; Coles & Tomporowski, 2008). Whilst it is possible that the exercise task may have influenced cognitive function and mood, studies that have induced dehydration through prolonged exercise similar to levels achieved in this study have been more commonly associated with deterioration in cognitive performance and mood state (Tomporowski, 2003; Grandjean & Grandjean, 2007; Lieberman, 2007; Shirreffs, 2009). There are some suggestions that adverse effects of dehydration on cognitive function and mood are likely with 2% or more reduction in hydration status (Grandjean & Grandjean, 2007; Shirreffs, 2009; Benton, 2011). The dehydration that occurred as a result of the exercise in this study may have affected participants' cognitive function and mood, decreasing their sensitivity to the effects of alcohol and resulting in reduced subjective ratings of confusion and intoxication. Further investigation into the effects of dehydration on subjective ratings of alcohol intoxication, impairment and bodily symptoms is required.

Alcoholic beverages are commonly consumed following events where dehydration is anticipated. Many people drink alcohol at the end of a sporting match or after a period of physical labour that causes fluid loss through sweating. The results from this study suggest that the body's

response to alcohol is not affected by dehydration producing a 2.5% loss in body weight, and peak concentrations of alcohol in the blood would be similar to conditions where dehydration was not present. However, other factors that typically occur as a result of physical activity or exertion such as increased body temperature and altered blood flow to the gastrointestinal tract and clearing organs may also impact on alcohol pharmacokinetics. In this study, participants were allowed to rest and cool down completely following the exercise component and prior to the ingestion of the alcoholic beverage. In reality, this may not always occur and often individuals consume alcohol shortly after physical activity when they may still have elevated body temperatures and possible altered blood flow to the organs integral to alcohol absorption and elimination. There is a need for further research examining other factors associated with exercise that may influence alcohol pharmacokinetics.

In summary, this study investigated the impact of dehydration on the blood and breath responses to a moderate dose of alcohol. Acute fluid loss as a result of exercise was shown to have no impact on alcohol pharmacokinetics including C_{max}, AUC, t_{max}, $t_{1/2}$, V_d, Cl, and MRT when group results were compared. However, large intra-individual variability in BAC and BrAC responses was observed across the two euhydration trials, which may have made it difficult to detect significant changes in pharmacokinetic variables under dehydrated conditions. There was some indication that dehydration may influence the subjective effects of alcohol, however further research examining the subjective effects of alcohol under different hydration conditions is required before definitive conclusions can be drawn. If dehydration does influence the subjective effects of alcohol, this may have direct implications for individuals who consume alcohol following physical activity and then consider driving.

Chapter Seven: Research Study Three - The Effects of Dehydration, Moderate Alcohol Consumption and Rehydration on Cognitive Functions

Reader's Note:

The information in this section has been published as an original research paper:

The co-authors of this publication confirm that the research candidate has made the following contributions to this study:

- Re-developed the study design.

- Completed the human research ethics application.

- Completed all participant recruitment and data collection.

- Conducted analysis of the data.

- Prepared manuscript for submission to journal.

- Presented research at a national and international conference.

Signed: _____   **Date: 06/09/13**

Signed: _____   **Date: 06/09/13**

Signed: _____   **Date: 06/09/13**

7.1 Abstract

Aim: This study investigated the impact of mild and moderate dehydration on alcohol-induced deteriorations in cognitive functions. **Methods:** Sixteen healthy males participated in a single-blind, placebo-controlled cross-over design study involving four experimental trials (separated by ≥7days). In each trial, participants were dehydrated by 2.5% BW through exercise. After a one hour recovery in a thermo-neutral environment (22±2°C, 60-70% RH) four tasks from the CANTAB were administered to the participants (Test 1). In two of the trials, participants were provided with water equivalent to either 50% or 150% BW loss. A set volume of alcohol or placebo was then consumed in each trial, incorporating the conditions: dehydration-placebo (DP), dehydration-alcohol (DA), partial rehydration-alcohol (PA), and full rehydration-alcohol (FA). The same four CANTAB tasks were then re-administered (Test 2). Subjective ratings of mood and estimates of alcohol intoxication and driving impairment were also recorded in each trial. **Results:** Alcohol consumption caused deterioration on three of the four CANTAB measures (viz., choice reaction time, executive function and response inhibition). This reduction in performance was exacerbated when participants were dehydrated compared to trials where full rehydration occurred. Subjective ratings of impairment and intoxication were not significantly different between any of the trials where alcohol was consumed; however ratings for alcohol trials were significantly higher than in the placebo trial. **Conclusions:** These findings suggest that rehydration after exercise that causes fluid loss can attenuate alcohol-related deterioration of cognitive functions. This may pose implications for post match fluid replacement if a moderate amount of alcohol is also consumed.

7.2 Introduction

Cognitive functions are critically important for many activities of daily living. Cognitive performance is influenced by many factors and can vary significantly over the course of a day or under various conditions (Newell et al., 2003). Alcohol consumption and dehydration are two factors shown to have a detrimental impact on cognitive performance (Fillmore, 2007; Grandjean & Grandjean, 2007). These factors have both received significant scientific attention.

Deterioration in performance following alcohol consumption has been shown on a range of cognitive tasks that include amongst others: measures of concentrated and divided attention (Moskowitz & Robinson, 1988; Moskowitz & Fiorentino, 2000); choice reaction time (Moskowitz & Fiorentino, 2000); response inhibition to stop-signal and go/no-go tasks (de-Wit et al., 2000; Marczinski et al., 2005; Fillmore, 2007); and tasks associated with executive function such as the TOL or SOC Test that involve spatial planning and motor control (Weissenborn & Duka, 2003). Some of this evidence has contributed to the development and application of blood alcohol limits for complex cognitive tasks such as driving motor vehicles and operating machinery. Generally, the degree of alcohol-related cognitive impairment occurs in a dose response manner (Moskowitz & Robinson, 1988) and the effects are obvious at high (>0.10%) BACs. Inconsistencies are reported in

the literature with low (<0.05%) to moderate (0.05-0.10%) levels of alcohol intoxication (Ogden & Moskowitz, 2004). However, this may reflect the lack of sensitivity in measures used during early studies to detect alcohol-induced changes in cognitive performance.

Evidence from studies using more sophisticated and sensitive assessment instruments suggests that driving related skills are impaired at any alcohol level departing from zero (Ogden & Moskowitz, 2004). In the review by Moskowitz and Fiorentino (2000), the authors found that over 94% of studies reported some skill impairment by BACs of 0.08%. More recently, Friedman et al. (2010) found that participants with mild intoxication (~0.05%) displayed a trend for slower responses and increased errors on a subtle cognitive impairment task compared to alcohol free control conditions. This task has been shown to correlate well with tests of choice reaction time and spatial working memory from neuropsychological testing instruments such as the CANTAB (Friedman et al., 2010).

The effects of alcohol have also been measured directly using the CANTAB instrument. Weissenborn and Duka (2003) used a CANTAB test of executive function (TOL/SOC) to examine spatial planning and motor control. The authors observed impairment in the number of trials completed in minimum moves, as well as an increase in initial thinking time and subsequent thinking time latencies when participants had consumed alcohol (mean BAC ~0.06%) compared to the alcohol-free control group. A number of studies have also demonstrated that measures of inhibitory control are reliably impaired by moderate (~0.06%) doses of alcohol (de-Wit et al., 2000; Marczinski et al., 2005; Fillmore, 2007). Using a stop signal task (SST) similar to that provided in the CANTAB, de-Wit et al. (2000) found that moderate doses of alcohol (~0.06%) impaired inhibition with significantly slowed stop signal reaction times (SSRT) observed.

The actions of alcohol on the brain are most likely due to its diverse effects on synaptic transmission involving a variety of neurotransmitters (Watson & Little, 2002). Alcohol has been shown to modulate the actions of neurotransmitters by altering the function of receptors, ion

channels, transporters and second messenger systems (Deitrich et al., 1989). Evidence from Positron Emission Tomography (PET) studies also suggest that alcohol influences cerebral blood flow, particularly to the cerebellum, which may be partly responsible for disruptions in functions such as fine motor coordination (Volkow et al., 1988).

Studies examining the impact of dehydration on cognitive function have indicated performance decrements (Grandjean & Grandjean, 2007; Lieberman, 2007). The impairment caused by dehydration has been associated with numerous cognitive abilities including attention (D'Anci et al., 2009), reaction time (Zuri et al., 2004), memory (Cian et al., 2000; Cian et al., 2001) and executive function (Gopinathan et al., 1988). It is generally accepted that reductions in cognitive performance are proportionate to the degree of dehydration and that cognitive impairment becomes detectable with fluid deficits greater than 2% body mass loss (Lieberman, 2007; Shirreffs, 2009). The performance deterioration that occurs as a result of dehydration is comparable to the impairment observed following alcohol consumption (Kenefick & Sawka, 2007). However, most studies induce dehydration through exercise methods in warm environments (Grandjean & Grandjean, 2007) and relatively few have investigated the effects of dehydration on cognitive performance independent of an applied heat stress (Cian et al., 2000; Cian et al., 2001).

The precise mechanism responsible for the adverse effects of dehydration on cognitive performance is still unclear. However, several mechanistic theories propose an integration of hormonal and cellular responses that directly affect the central nervous system through changes in neuronal function and neurotransmission (Wilson & Morley, 2003). Recent evidence also suggests that dehydration causes structural and functional brain alterations (decreased brain volume, increased ventricular system, alterations in blood flow) that may interfere with normal cognitive functioning (Kempton et al., 2009; Kempton et al., 2011).

At present, studies have only considered the effects of dehydration and alcohol consumption on cognitive performance separately. No literature currently exists investigating cognitive

performance when moderate alcohol consumption is combined with mild or moderate levels of dehydration. Many people consume alcoholic beverages following activities that are physically demanding. They are also likely to experience a period of rest or cooling after physical activity and prior to cognitive demand. The consumption of alcohol under conditions where dehydration is anticipated may be further detrimental to cognitive performance, given the overlap in proposed mechanistic actions on the central nervous system such as changes in neurotransmitter actions and altered blood flow. In addition, dehydration causes protein-free filtrate to leave the bloodstream, resulting in a reduction of absolute blood volume (Harrison, 1985). Alcohol distributed throughout the body via reduced blood volume may cause a greater concentration of alcohol to infiltrate the brain, which could consequently result in an amplification of alcohol's effects on cognitive function. Ultimately, this could influence an individual's ability to carry out every day tasks such as driving a motor vehicle or operating machinery.

The aim of this study was to investigate if mild or moderate dehydration combined with moderate alcohol consumption causes greater impairment in cognitive functions compared to the consumption of alcohol under fully rehydrated conditions following exercise. It was hypothesised that the alcohol induced effects on cognitive performance would be greater when participants were dehydrated compared to those observed during rehydration trials. This may have direct implications for the safety of individuals operating motor vehicles following physical exertion and subsequent permissible alcohol consumption.

7.3 Materials and Methods

Participants

Sixteen healthy untrained males (22.7±3.3 yrs, 77.28±9.13 kg BW, 176.7±5.7 cm, VO_2 peak 43.0±4.7 ml/kg/min; values are mean±SD) volunteered to participate in this study. Participants had a regular history of alcohol consumption of 5.2±3.7 yrs. The self-reported intake of alcoholic

beverages was equivalent to 5.9±2.6 standard drinks (based on the consumption of alcohol from a range of sources including beer, wine and spirits that contain 10g of ethanol) and drinking frequency was reported as 1.8±1.6 times per week using the personal drinking history questionnaire (Vogel-Sprott, 1992). All participants were fully informed of the nature and possible risks of the study before giving their written informed consent. The investigation was approved by Griffith University's Human Research Ethics Committee (PBH/01/10/HREC) and the procedures were conducted in accordance with the principles outlined by the agreement of Helsinki.

Preliminary testing

Each participant visited the laboratory on five occasions. The first visit involved preliminary screening for eligibility and a test to assess participants' maximal exercise capacity. Each volunteer completed a questionnaire that provided demographic information, drinking habits, drug use and physical and mental health status. Individuals with a self-reported psychiatric disorder, substance abuse disorder, head trauma, or other CNS injury were excluded from the study. As an additional screen for alcohol dependence, volunteers with a score of five or higher on the Short-Michigan Alcoholism Screening Test (S-MAST) (Selzer et al., 1975) were also excluded from the study. Eligible participants then performed an incremental test to exhaustion (VO_2 peak test) on an electromagnetically braked cycle ergometer (Lode Instruments, Groningen, The Netherlands) to determine VO_2 peak. Briefly, each test began at 100W and increased in 25W increments every 2.5 min until exhaustion. During the VO_2 peak test, which typically lasted between 20 and 25 min, expired air was continuously analysed by a calibrated metabolic measurement system (MedGraphics, Minnesota, USA). At the end of the test a familiarisation with the cognitive testing instrument and procedures was performed. Participants were given verbal instructions and practised each of the cognitive tasks until they were comfortable with the procedures.

Experimental design

Each participant undertook four experimental trials (Fig. 7a). The trials were completed using a single-blind administration protocol and the four experimental treatments were randomised via an incomplete Latin square design.
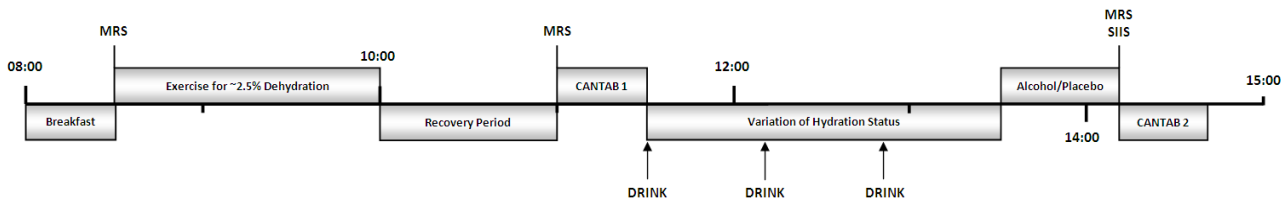

Fig. 7a. Experimental protocol design. Each participant underwent four experimental sessions. CANTAB 1 and 2 correspond to the two cognitive performance assessments. MRS refers to administration of the mood rating scale. SIIS refers to the administration of the subjective intoxication and impairment scale. Drink corresponds to rehydration trials where 50% (P, partial) or 150% (F, full) of fluid loss is replaced.

Pre-Experimental Procedures

Experimental trials were separated by at least seven days and were conducted at the same time of the day in a stable laboratory environment ($22\pm2^{\circ}$C, 60-70% RH). Participants were asked to abstain from alcohol for 24hrs, and caffeine-containing substances and moderate-strenuous exercise for 12hrs prior to each experimental trial. During the 24hr period immediately preceding the first trial, participants recorded all food and beverages consumed as well as any exercise completed. A food and exercise record with this information was supplied to each participant and they were asked to repeat this on the day prior to all subsequent trials. On the morning of each trial participants were provided with a standardised meal for breakfast (Energy = 19.8 ± 0.6 KJ/kg BW, CHO = 0.9 ± 0.0 g/kg BW), consumed 30 min prior to commencing the trial and included fruit bread, jam, margarine and 125ml of apple juice. All dietary preparation and analysis was performed using Foodworks® Version 6.0, 2009, (Xyris Software, Australia) dietary analysis software.

Experimental procedures

Participants arrived at the laboratory fasted between ~07:00-08:00hrs. Compliance to pre-experimental conditions was verbally acknowledged on arrival and a measure of BrAC was taken to verify a zero alcohol reading. A urine sample was then collected to calculate U_{sg} as an initial measure of hydration status. Participants who recorded a U_{sg} reading >1.020, indicating some level of pre-existing hypo-hydration were provided with additional water until a urinary sample fell below the acceptable threshold. Eight participants required water (500-1500ml) on a total of 13 occasions. The fluid was consumed over 30 min, followed by a 30 min rest period, before subsequent U_{sg} measurements were taken. Baseline measures of tympanic temperature (T_t; Braun ThermoScan®, Welch Allyn) were then taken and a baseline blood glucose (BGL) measure was recorded using a finger prick sample (Accuchek Advantage II®, Roche) before participants were provided with the standardised breakfast to consume in 30 min. Immediately following breakfast participants completed a subjective mood rating scale (MRS) questionnaire (Bond & Lader, 1974) using a computerised VAS (Marsh-Richard et al., 2009). Participants were then asked to void their bladder completely and an initial nude body weight was measured.

After the body weight measurement, dehydration was induced by intermittent exercise on a cycle ergometer (Monark, Ergomedic 828E, Vansbro, Sweden) at an intensity corresponding to ~60% VO_2 peak. During the exercise ride, participants wore warm clothing and commercial disposable coveralls to assist with sweat loss. Five minute periods of exercise were separated by one minute rest periods. The intention was to induce dehydration equivalent to 2.5% body mass loss. Participants would stop exercise once they had reached ~2.3% body mass loss or after a total of 90 min exercise, whichever occurred first. Body weight was measured at the end of 60 min of exercise and at 10 min intervals thereafter to determine fluid loss. At the end of exercise a measure of T_t and nude body weight was recorded before participants took a cool shower. After the shower, participants dried themselves thoroughly and a nude body mass measurement was

taken before they rested for a period of one hour. At the end of the recovery period, a second MRS was completed and measures of T_t and BGL were recorded.

Following the recovery period, a four task protocol from the CANTAB was completed (Test 1), which lasted for ~30 min. On completion of the test battery, participants were either provided with no water (D), a small amount of water equivalent to 50% body mass loss (P), or a large amount of water equivalent to 150% body mass loss (F) consumed as 3 drinks, 20 min apart and in volumes equivalent to 50%, 33% and 17% of the total fluid volume. In addition, participants received 50mmol/L of sodium (given as NaCl capsules) in trials where water was consumed. Nude body weight was recorded each hour during the rehydration stage for all trials. Immediately prior to providing measures of nude body weight, participants were asked to void any urine, which was collected in containers and subsequently weighed to calculate cumulative urine loss.

Following the rehydration phase, participants consumed a set volume of alcohol (A) or placebo (P) to incorporate the conditions dehydration-placebo (DP), dehydration-alcohol (DA), partial rehydration-alcohol (PA) and full rehydration-alcohol (FA). Alcohol was administered as vodka (Smirnoff®, 37% v/v ethanol) mixed as a beverage described in Pilot Study One (Chapter 4.2). The volume of the alcoholic beverage was individually calculated and intended to raise BrAC to ~0.05% (Watson, et al., 1981). This dose was selected as it reflects the current legal maximum blood alcohol limit for operating a motor vehicle in Australia. The placebo beverage was made as per the description in Pilot Study One (Chapter 4.2). Participants were not informed of a placebo trial and expected to receive alcohol in all trials. All drinks were prepared in front of the participant and a vodka bottle was filled with water for the purpose of preparing the placebo beverage. Participants were asked to consume each drink at a steady pace over 10 min. Following consumption they rinsed their mouths with water to minimise residual mouth alcohol. At the time of drinking the beverage, participants were asked to complete a tasting questionnaire as a measure of expectancy manipulation. The questionnaire has been described in detail in Pilot Study One (Chapter 4.2).

Breath alcohol concentrations were analysed using a police grade Alcolizer LE breathalyser (Alcolizer Pty Ltd) with measurements taken 15 min and 30 min post ingestion. All BrAC measurements were taken in duplicate, with a triplicate measure recorded if readings differentiated by ≥0.005%. The measures were averaged to provide the final assessment of BrAC. Participants were not informed of their BrAC measures until after completion of the entire study. Just prior to the 30 min BrAC sample, a final MRS and a subjective impairment and intoxication scale (SIIS) were completed using computerised VAS questionnaires. A final BGL was also taken at this time. Immediately after the 30 min BrAC sample, the same four tasks from the CANTAB were administered (Test 2) before a final BrAC, urine volume and body weight were recorded (~60 min post ingestion).

Cognitive tasks (CANTAB)

Assessment of cognitive performance was completed using the four task CANTAB test battery described in Pilot Study Three (Chapter 4.4). Many studies support the validity and use of neuropsychological assessment with the CANTAB (Lange et al., 1992; Robbins et al., 1994; Fray & Robbins, 1996; Fowler et al., 1997; Robbins et al., 1998; Louis et al., 1999; Weissenborn & Duka, 2003; Egerhazi et al., 2007). The CANTAB tasks were chosen on the basis of their established sensitivity to the disruptive effects of alcohol as demonstrated in previous research (de-Wit et al., 2000; Weissenborn & Duka, 2003; Friedman et al., 2010), and to examine cognitive domains that are likely to be relevant to driving related skills.

Subjective ratings

Adaptive Visual Analogue Scales (AVAS) were used to assess mood (Bond & Lader, 1974) and subjective ratings of intoxication and impairment (Fillmore, 2001; Harrison et al., 2007). Each scale

was administered using a computerised modifiable software program, AVAS (Marsh-Richard et al., 2009) on the screen of a laptop computer.

Mood rating scale

The mood rating scale consisted of six separate analogue scales. These scales have been used in previous research and relate to a factor of mood representing alertness (Bond & Lader, 1974). Participants were presented with a 100mm line, the ends of which were marked with antonyms (alert-drowsy, confused-clearheaded, well coordinated-clumsy, lethargic-energetic, interested-bored, incompetent-competent), and they adjusted the position of a cursor on each line using a mouse to indicate how they felt at that moment. The score was taken as the cursor position based on percentage of scale length.

Subjective impairment and intoxication scale

The degree of subjective impairment and intoxication was measured on four separate 100mm visual-analogue scales. Participants rated intoxication by how much they "feel the effects of alcohol" between anchors of 'not at all' and 'very much'. Subjective impairment was estimated based on the degree to which participants felt their driving performance was impaired after drinking. Ratings were obtained on a scale between 'no impairment' and 'extreme impairment'. Two other driving-related questions were used to ascertain: (a) "How able are you to drive a car at this time?" and (b) "How willing are you to drive a car at this time?" Ratings were reported between 'not at all' and 'very much'. These scales have been used in other studies of alcohol and driving and are sensitive to the effects of the drug (Fillmore, 2001; Harrison et al., 2007; Fillmore et al., 2008).

All statistical procedures were performed using SPSS for Windows, Version 19.0 (SPSS Inc., Chicago, IL). Planned comparisons were performed to test our specific hypothesis that alcohol induced effects on cognitive performance would be greater when participants were dehydrated compared to those observed during rehydration trials. In this case, statistical analysis for each of the main dependent variables on CANTAB tasks was conducted using paired samples *t*-tests to compare Test 1 (T1) and Test 2 (T2) responses for each trial. Comparisons between trials were conducted using one-way repeated-measures ANOVA and pairwise comparisons (LSD) were performed where significant main effects were present. Scores derived from the MRS were subjected to a two-way ANOVA; Protocol (DP, DA, PA, FA) x Time (first, second, third), with both as repeated measures factors. Post hoc analysis (LSD) was performed on all significant *F* ratios ($p<0.05$). All other measures were analysed by one-way repeated-measures ANOVA, and pairwise comparisons (LSD) were performed where significant main effects were present. Statistical significance was accepted at $p<0.05$. All data are reported as mean±standard deviation unless otherwise specified.

7.4 Results

Trial drink ratings

Under all trial conditions participants rated the beverage as having a low to moderate amount of alcohol, which indicates that the placebo beverage was effective in establishing a belief that alcohol had been received. There was no difference in certainty of perception between the trials, with participants reporting mean certainty ratings between 'somewhat' and 'very' certain under all conditions. Only one participant was able to identify the placebo beverage as having no alcohol at the time of drinking. This participant was 'very certain' in their perceptions.

Cognitive performance measures

Choice Reaction Time (CRT). A significant increase in latency was observed for DA and PA trials ($p<0.05$) with no differences noted between the tests for both DP and FA trials. The percentage of correct responses showed no significant variation between tests regardless of trial conditions. Participants had a high degree of success (>98% correct) in response selection to stimuli across both testing stages in all trials (Fig. 7b).
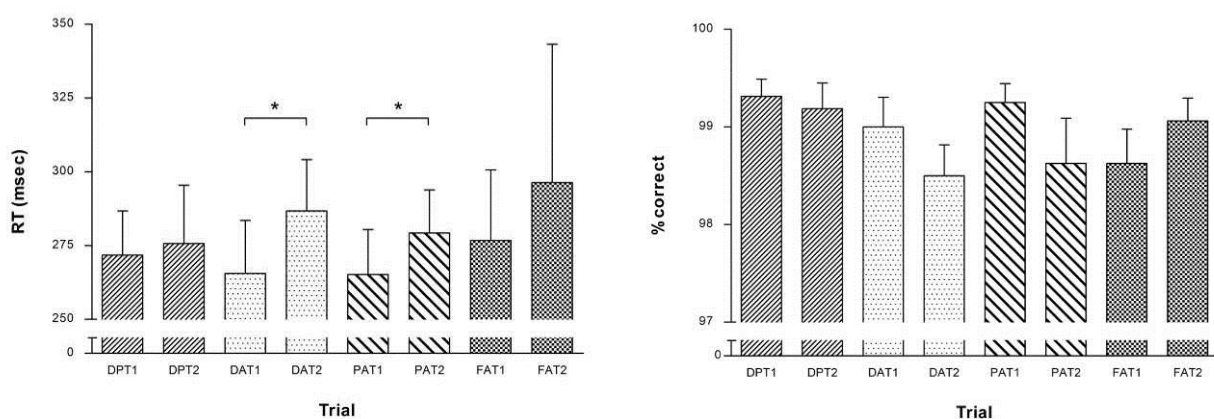
Fig. 7b. CRT latency and response accuracy for each trial. *Significant difference between T1 and T2 results ($p<0.05$).

Match To Sample (MTS). No significant differences were observed for reaction time, movement time or response rate between tests in any of the trials on this task (Fig. 7c; $p>0.05$). The mean reaction time in this task was considerably longer than the CRT task due to the visual search and match requirements of the test (1445±454ms). Mean movement time was 460±176ms and the proportion of correct responses was high (93.2±6.4%) across all trial conditions. This task was not sensitive to the conditions employed across trials in this study.

Fig. 7c. MTS reaction time and response accuracy for each trial.

Stop Signal Task (SST). Differences in stop signal reaction time (SSRT) and number of direction errors made are illustrated in Fig. 7d. There was a significant difference in SSRT between tests for the DA trial, with a slower response recorded after ingestion of alcohol ($p<0.05$). No difference was seen in any of the other conditions ($p>0.05$). There was no difference between tests for the proportion of successful stops made in any of the trials ($p>0.05$). Significantly more direction errors were made during Test 2 for both DA and FA trials compared to test 1 ($p<0.05$).

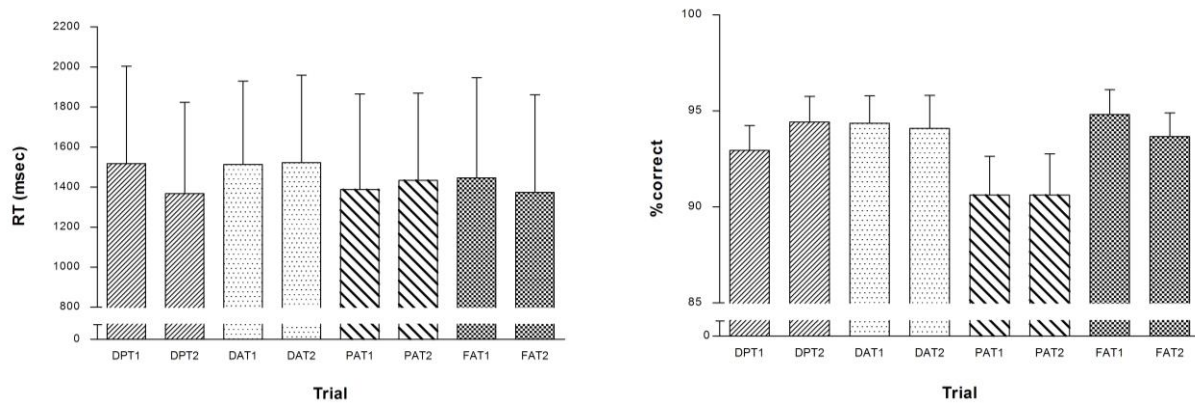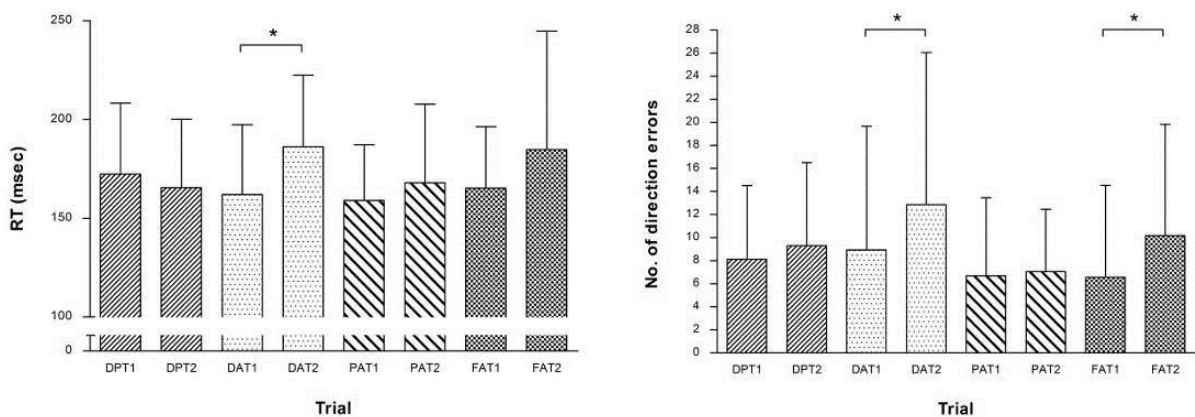**Fig. 7d.** SST mean reaction time and number of direction errors made for each trial. *Significant difference between T1 and T2 results ($p<0.05$).

Stockings of Cambridge (SOC). A significant difference in the number of problems solved in minimum number of moves was observed for the FA trial ($p<0.05$) with no differences between tests in any of the other trials (Fig. 7e). No differences were observed in the mean number of

moves required for n=2, 3 or 4 move tasks across any of the conditions, however a significant reduction in the number of moves required to complete n=5 move task was observed in Test 2 of the FA trial. No differences were recorded for the n=5 move task in any other trials (p>0.05).
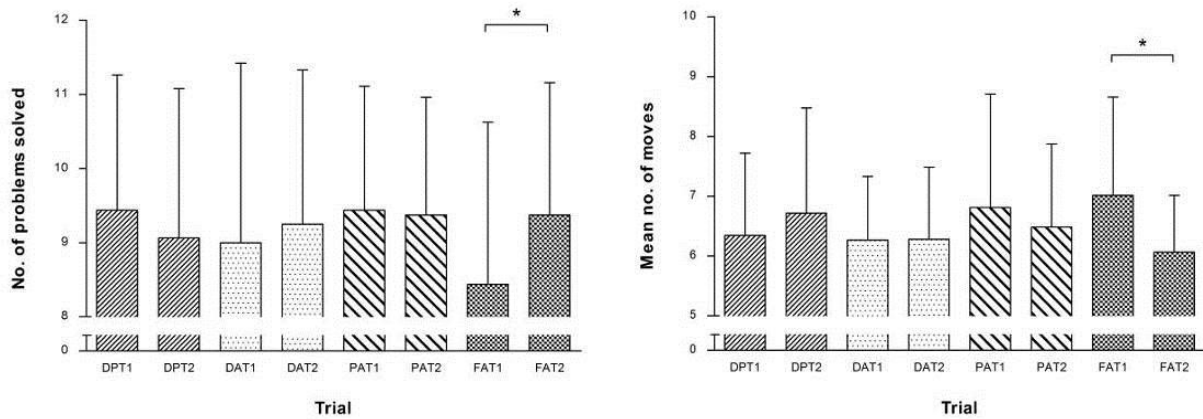
Fig. 7e. SOC mean number of problems solved in minimum moves and the mean number of moves required to complete the n=5 move task for each trial. *Significant difference between T1 and T2 results (p<0.05).

Levels of hydration and body mass changes

The dehydration protocol was successful in achieving similar levels of body mass loss between trials (Table 7a). Significant differences in body mass were recorded between trials after rehydration (p<0.05). These differences remained significant with the final body weight measurement taken after CANTAB Test 2 (p<0.05).

Table 7a. Mean body weight loss (%) compared with initial body weight measure for each trial (n=16)

Trial	Mean percentage of body mass loss/gain (%)		
	After dehydration protocol	After rehydration protocol	After CANTAB (test 2)
DP	-2.40 ± 0.31	-2.75 ± 0.31	-2.29 ± 0.41
DA	-2.39 ± 0.32	-2.71 ± 0.30	-2.42 ± 0.33
PA	-2.31 ± 0.26	-1.54 ± 0.27 *	-1.41 ± 0.38 *
FA	-2.47 ± 0.29	+0.19 ± 0.49 *	-0.56 ± 0.63 *

*Significant difference from all other trials. Values are mean±SD.

Mood rating

A number of significant effects were found on measures derived from the MRS questionnaires (Fig. 7f). On the alert-drowsy scale, there was a significant main effect for time, $F_{(2,30)}=4.23$; $p=0.024$, but no effect of protocol, $F_{(3,45)}=1.20$; $p=0.322$, or protocol x time interaction, $F_{(6,90)}=0.59$, $p=0.740$. Post hoc analysis revealed higher ratings of drowsiness at time three compared to time one ($p<0.05$). For the confused-clear headed scale, there was a significant main effect for time, $F_{(2,30)}=14.18$; $p<0.01$, with higher ratings of confusion at each subsequent time point ($p<0.05$), but no effect of protocol, $F_{(3,45)}=1.56$; $p=0.212$, or protocol x time interaction, $F_{(6,90)}=1.58$; $p=0.163$. On the well coordinated-clumsy scale, there was a significant main effect for both protocol, $F_{(3,45)}=3.38$; $p=0.026$, and time, $F_{(2,30)}=16.38$; $p<0.01$, but no protocol x time interaction, $F_{(6,90)}=1.49$; $p=0.192$. Post hoc analysis revealed higher levels of clumsiness at each subsequent time point and on all alcohol trials compared to the placebo trial ($p<0.05$). For the incompetent-competent scale, there was a significant main effect for time, $F_{(2,30)}=8.48$; $p=0.01$, with higher levels of incompetence reported in tests two and three compared to test one ($p<0.05$), but no effect of protocol, $F_{(3,45)}=0.18$; $p=0.909$, or protocol x time interaction, $F_{(6,90)}=1.92$; $p=0.087$.

There were no significant main effects of protocol, $F_{(3,45)}=1.003$; $p=0.400$, time, $F_{(2,30)}=2.69$; $p=0.084$, or protocol x time interaction, $F_{(6,90)}=0.305$; $p=0.933$, observed for the lethargic-energetic scale, indicating that participants' CANTAB results were not influenced by fatigue. Likewise, there were no significant main effects found on the interested-bored scale for protocol, $F_{(3,45)}=1.79$; $p=0.164$, time, $F_{(2,30)}=3.13$; $p=0.058$, or protocol x time interaction, $F_{(6,90)}=1.97$; $p=0.079$, indicating that trial results were not influenced by boredom.
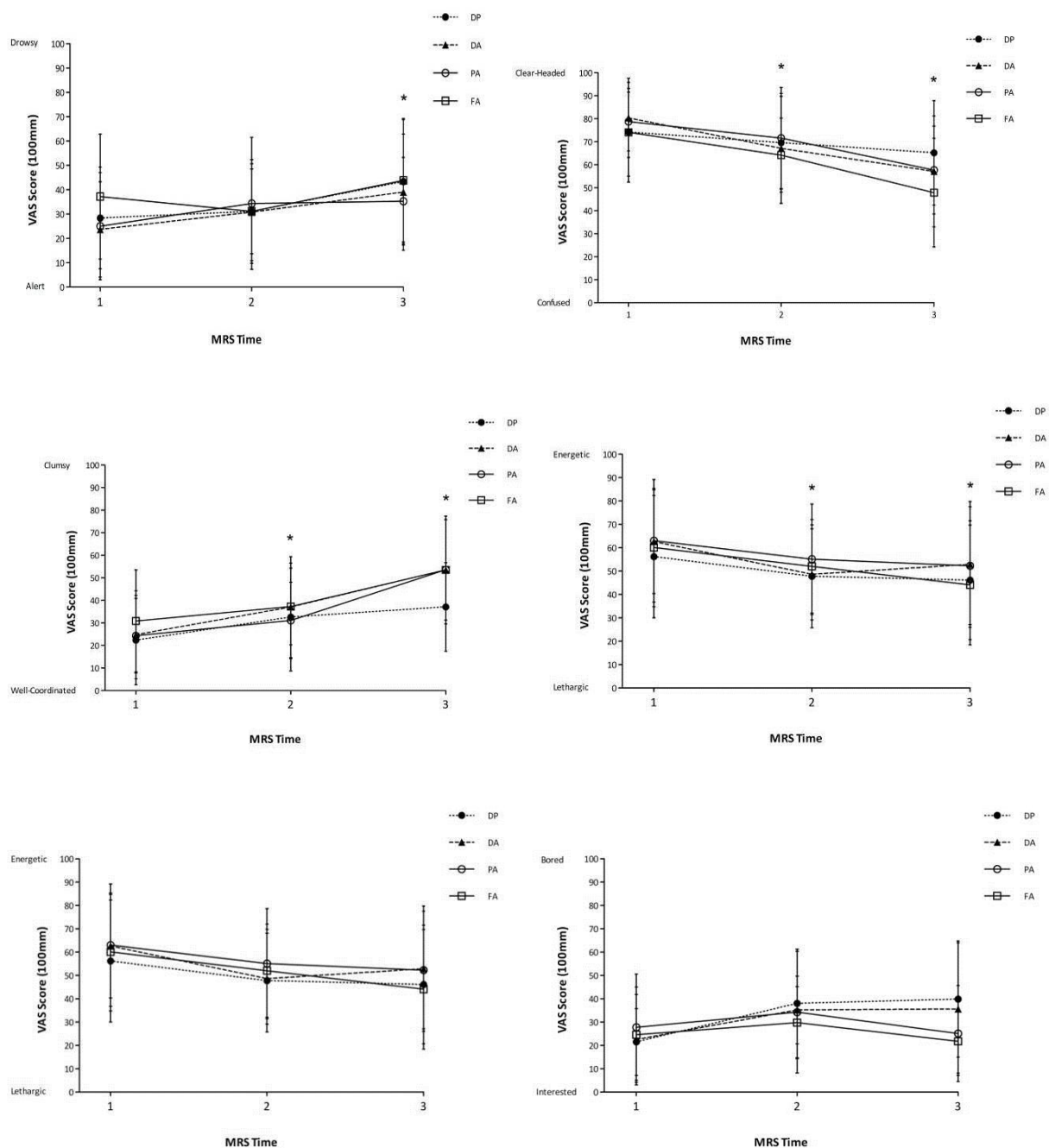
Fig. 7f. Mood Rating Scale VAS scores. Alert - Drowsy, Confused - Clear-Headed, Well-Coordinated - Clumsy, Incompetent - Competent, Lethargic - Energetic, Interested - Bored. *Significant difference between times, protocols, or trials; see text for details ($p<0.05$).

Subjective intoxication and perceived ability to drive

Participants' subjective ratings of alcohol effects and level of impairment were not different between the three alcohol trials (Fig. 7g). Ratings for the placebo trial were significantly lower than alcohol trials ($p<0.05$), however there was still some indication of alcohol effects and impairment reported for the placebo trial with mean values on these scales greater than zero. Participants

reported that they were less able and less willing to drive a car following alcohol consumption compared to placebo, irrespective of hydration status ($p<0.05$).
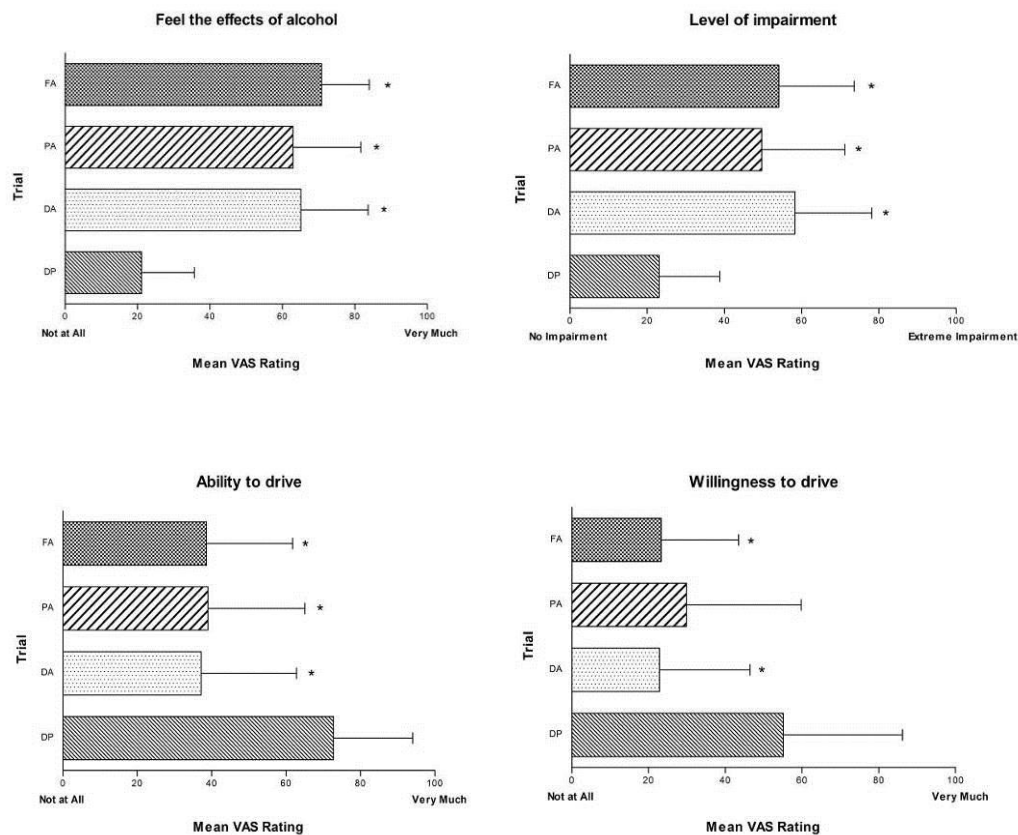
Fig. 7g. Subjective ratings of alcohol effects, level of impairment, ability to drive and willingness to drive a car for each trial. *Significant difference compared to placebo trial ($p<0.05$).

Physiological measures

Summary data for physiological measures taken throughout testing are presented in Table 7b. Tympanic temperature increased significantly with exercise ($p<0.05$). The post exercise recovery period was effective in cooling, with T_t measures taken prior to CANTAB Test 1 similar to pre-trial measures. A significant difference was recorded between CANTAB Test 1 and pre-trial measures for the DP and PA trials ($p<0.05$), however the differences were not considered clinically significant and were within the error margins indicated for accuracy of the tympanic device (±0.2°C). Blood glucose responses did not differ between pre-trial and CANTAB Test 1 measures. There was a general trend for blood glucose levels to decrease over time in all trials after exercise ($P≤0.05$).

However, values recorded on final measures taken prior to CANTAB Test 2 were still within the accepted range for normal glycemia (Diabetes Australia, 2009).

Table 7b. Summary data for physiological measures for each trial (n=16)

	DP	DA	PA	FA
Tympanic temperature (°C)				
Pre-trial	36.1 ± 0.3	36.2 ± 0.3	36.1 ± 0.4	36.2 ± 0.3
Post exercise	37.1 ± 0.5 [#]	37.1 ± 0.5 [#]	37.2 ± 0.5 [#]	37.2 ± 0.5 [#]
CANTAB (Test1)	36.4 ± 0.3 [*]	36.3 ± 0.4	36.3 ± 0.5 [*]	36.3 ± 0.4
Blood glucose level (mmol/L)				
Pre-trial	6.1 ± 0.6	6.1 ± 0.5	6.3 ± 0.4	6.2 ± 0.4
CANTAB (Test 1)	6.1 ± 0.6	5.7 ± 0.6	6.2 ± 0.9	6.0 ± 0.6
CANTAB (Test 2)	5.6 ± 0.5 [#]	5.5 ± 0.5 [*]	5.7 ± 0.5 [#]	5.5 ± 0.5 [#]

*Significant difference from pre-trial measures ($P \leq 0.05$). #Significant difference from pre-trial and CANTAB (test 1) measures ($p < 0.05$). Values are mean±SD.

Breath alcohol concentrations (BrACs)

No significant difference in BrAC was recorded between trials at any of the measured time points ($p < 0.05$). Peak BrACs were achieved 15-30 min post alcohol ingestion with mean levels of 0.072±0.017%, 0.074±0.017%, and 0.072±0.015% for the DA, DP and FA trials respectively. As expected, no measurable breath alcohol was detected for the DP trial (Fig. 7h). Cognitive tasks were performed between 30 and 60 min after drinking. Final BrACs measured at the end of CANTAB Test 2 revealed that the task was performed when alcohol concentrations were descending, with small but significant reductions (0.063±0.009%, 0.064±0.005%, and 0.060±0.006% for DA, PA, and FA trials respectively) noted in all trials ($p < 0.05$).
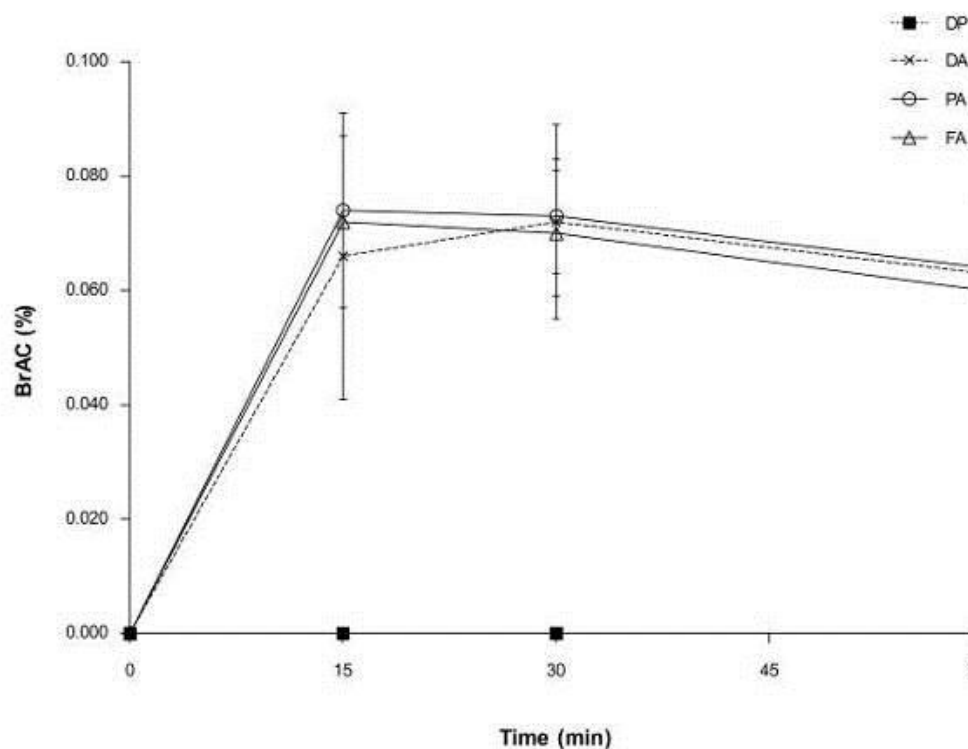
Fig. 7h. Breath alcohol concentration post beverage administration for each trial. *Significant difference from BrAC at time 30min ($p<0.05$). Values are mean±SD.

7.5 Discussion

To our knowledge this was the first investigation to examine the impact of exercise induced dehydration and moderate alcohol consumption on cognitive performance parameters including choice reaction time, executive function and response inhibition. The findings of this study indicate that mild to moderate dehydration causes greater deterioration in some cognitive functions in individuals who have consumed alcohol compared to conditions where fluid deficit is corrected.

On the CRT task an increase in latency was observed after alcohol was consumed in trials where participants were dehydrated (DA) and partially rehydrated (PA) in comparison to the full rehydration (FA) and placebo (DP) trials, whilst the trials did not differ with regard to the number of correct responses made. Alcohol administration in doses that elicit concentrations above 0.060% have shown consistent impairing effects on CRT tasks in previous research (Maylor & Rabbitt, 1993; Moskowitz & Fiorentino, 2000). However, studies specifically investigating the

187

impact of dehydration on CRT tasks have typically not found effects (Cian et al., 2000; Cian et al., 2001; Neave et al., 2001; Szinnai et al., 2005; McMorris et al., 2006; Serwah & Marino, 2006; D'Anci et al., 2009; Armstrong et al., 2012) and these tasks are often referred to as being insensitive to dehydration. The results from this study are inconsistent with previous investigations of dehydration on CRT latency performance. The findings suggest that reduction in CRT latency as a result of exercise induced dehydration and alcohol consumption can be reversed if sufficient fluid consumption occurs. Alcohol has a known ability to impair performance, which was observed during trials in this study where alcohol was administered (DA, PA). The reduced impairment that occurs following adequate rehydration (FA) in this study may provide evidence for the effects of dehydration on CRT tasks. It may, however, also be a result of dehydration causing a greater alcohol interaction and the effects cannot solely be attributed to dehydration. In agreement with previous research, the results from this study show no effect of hydration status on accuracy during the CRT task (Cian et al., 2000; Cian et al., 2001). There is some evidence to suggest that a speed-accuracy trade-off occurs on CRT tasks following the consumption of alcohol (Maylor et al., 1987). The results of this study appear to support this model, with no differences observed in CRT accuracy on any of the trials, whilst an increase in latency was seen following alcohol ingestion in trials where adequate rehydration was not provided.

Performance on the SST task revealed an impact of hydration status on SSRT, while no effect was seen on inhibitory control (proportion of successful stops) following alcohol administration. Stop-signal reaction time was significantly increased after alcohol consumption when participants were in the dehydrated condition (DA) compared to the placebo (DP) and both rehydration trials (PA, FA). Studies using response inhibition tests such as the stop-signal or go/no-go tasks have consistently found impairment following moderate (BACs >0.05%) alcohol consumption (Guillot et al., 2010). However, there is a lack of published research describing the effects of dehydration on these tasks. The SSRT results observed in this study support the work of Loeber and Duka (2009)

who also found alcohol caused an increase in SSRT. No comparison can be made with the proportion of successful stops as inhibitory control was not measured in their study, however, others have suggested that inhibitory control may be more sensitive to the disruptive effects of alcohol than response time based measures (Mulvihill et al., 1997). A slower SSRT observed with alcohol after dehydration in this study may have allowed more time to inhibit responses, resulting in no difference to the proportion of successful stops between tests or compared to other trials. The slower SSRT observed with dehydration and alcohol is reversed when rehydration takes place, with no effect on inhibitory control. This suggests that hydration status may be equally important as that of alcohol as a cause of impairment on response inhibition tasks, particularly in SSRT. However, while SSRT was maintained on the FA trial, more direction errors were recorded suggesting a trade-off between speed and accuracy on this task. Further research is required to clarify the impact of dehydration and alcohol consumption on response inhibition capabilities.

Measures of executive function other than response inhibition have previously been shown to be affected by the acute administration of alcohol in doses that elicit BrACs similar to those achieved in this study (Lyvers & Maltzman, 1991; Weissenborn & Duka, 2003). In contrast, some studies have revealed no alcohol induced impairments on executive function tasks (Peterson et al., 1990). Inconsistent results have also been reported in studies examining the effects of dehydration on executive function (Gopinathan et al., 1988; Kempton et al., 2011). The inconsistency may be due to methodological differences employed such as the dehydration intervention (i.e. heat and exercise or isolated exercise), the level of dehydration induced and the use of different tests to measure executive function in these studies. Results from the present study indicate no effect of alcohol on SOC performance measures for the number of problems solved in minimum moves or the mean number of moves required to complete n move tasks. There is, however, an effect of hydration status on these performance measures with more problems solved in minimum moves and fewer moves required to complete the n=5 move task on

the full rehydration (FA) trial Test 2 compared to Test 1 measures. These effects were not seen with SOC tasks that required fewer moves to complete (*n*=2, 3 or 4 moves) and suggests that impairment on executive function tasks as a result of dehydration may be dependent on task complexity and difficulty. However, it is important to acknowledge that the SOC task may be susceptible to practice effects. Thus performance improvements observed on the FA trial condition and/or the lack of effect of other trial conditions on SOC performance may have been a result of a learning effect. Like many tests of executive function, practice effects can lead to a strategy being acquired in the SOC task.

Overall, the results of this study indicate that dehydration through sweat loss in combination with moderate alcohol consumption has detrimental effects on some cognitive functions. However, these effects were not uniform across all of the cognitive tasks employed in this study and further research is required in order to clarify tasks that may be more susceptible to the combined effects of alcohol and dehydration. Where interactive effects were observed, a reduction in task impairment occurred when adequate rehydration occurred. These findings may apply to situations where people consume permissible amounts of alcohol following physical exertion that causes dehydration, and then undertake cognitive demanding tasks such as the operation of a motor vehicle.

Interestingly, dehydration did not have any effect on measures of breath alcohol concentration in this study. It is often assumed that being dehydrated will cause higher BrAC levels due to lower levels of total body water and reduced dilution of alcohol in the body tissues. The fact that BrAC levels did not differ in this study indicates that the differences in cognitive impairment observed between trials were not due to variations in alcohol concentration as a result of subtle changes in total body water content. Additionally, subjective ratings of intoxication and impairment to alcohol were not different between trials on the effects experienced or the level of impairment reported following alcohol consumption under all hydration conditions. This suggests that factors

such as hydration status may influence the alcohol interaction in the brain. A combination of dehydration and alcohol consumption could mediate deteriorations in cognitive performance through interactive effects on neuronal activity and the expression of neurotransmission (Deitrich et al., 1989; Wilson & Morley, 2003). There is a need for further research examining the effects of dehydration and alcohol consumption on cognitive performance to understand these interactions.

Alcohol and dehydration have independently been shown to influence subjective ratings of mood (Lex et al., 1988; Heishman et al., 1997; Lieberman, 2007; Shirreffs, 2009). Generally, these are both associated with a deterioration in mood state. However, alcohol in low doses has been shown to improve mood state (Lloyd & Rogers, 1997) and subjective ratings may be influenced by individual differences in alcohol expectancy and environmental settings (Sher, 1985). One could speculate that moderate alcohol consumption under conditions of dehydration would result in greater impairment to mood state than when these conditions are isolated. However, in this study no effect of protocol condition was observed on subjective ratings of mood. Participants' ratings of confusion and clumsiness were increased after the consumption of alcohol regardless of hydration status, which may suggest that the effects of alcohol outweigh the effects of dehydration on mood state. Given that performance on some cognitive tasks was influenced under the combined conditions of alcohol and dehydration, it appears that this was not caused by a change in subjective perception of effects from the trial condition.

One of the limitations of the current study is that the study design did not include placebo protocols for the partial rehydration and full rehydration trials. It is therefore difficult to make accurate conclusions about the relative effects of hydration and alcohol on cognitive performance because the effects of alcohol and level of dehydration on cognitive function cannot be readily separated. Whilst it was not the intention of this study to investigate dose response effects, incorporation of a placebo arm under different hydration conditions may supplement these findings. However, another potential limitation of the study is that it compares an alcohol prime

(DA) with a placebo (DP). It is possible that the anticipated effects of alcohol could have a drug like effect (Stewart et al., 1984; Hull & Bond, 1986) or a drug opposite effect (Siegel, 1999; Siegel, 2005) that could increase or decrease the magnitude of differences between the DP and DA conditions. Thus, any null findings between the DA and DP conditions could be the result of a drug like response to the placebo and significant differences could be due to a drug opposite response. A final limitation of this study is that the executive function task used (SOC task) is likely to be susceptible to practice effects through changes in strategic planning as trials progressed. The inability to observe changes in performance in this task on the DA trial may have been exaggerated due to the possible effect of practice. Careful consideration of performance tasks is required to ensure that results are not confounded by these conditions in future studies.

In summary, this study investigated the impact of mild and moderate dehydration combined with moderate alcohol consumption on measures of cognitive function. The effects of alcohol and dehydration/rehydration were not uniform across all of the tasks measured in this study and it appears that dehydration does not produce systematic effects on impairment caused by alcohol intoxication. Further research is required to clarify the cognitive tasks that may be more susceptible to the combined effects of alcohol and dehydration. Whilst varied results were observed for the effects of alcohol and dehydration on measures of spatial planning, response inhibition and attention, the cognitive impairment observed after dehydration and moderate alcohol consumption on tasks involving choice reaction time appears to be no longer present when adequate rehydration occurs. These findings may have direct implications for individuals involved in physical activity that results in fluid loss through sweating, particularly if permissible alcohol consumption also occurs prior to activities that involve these cognitive parameters, such as the operation of a motor vehicle.

Chapter Eight: Research Study Four - The Effect of Dehydration, Moderate Alcohol Consumption and Rehydration on Simulated Driving Performance

Reader's Note:

The information in this section has been published as an original research paper:

Irwin C, Shum D, Leveritt M, Desbrow B. Mild to moderate dehydration combined with moderate alcohol consumption has no influence on simulated driving performance. *Traffic Injury Prevention*, 2013; (In Press).

The co-authors of this publication confirm that the research candidate has made the following contributions to this study:

- Developed the study design.

- Completed the human research ethics application.

- Completed all participant recruitment and data collection.

- Conducted analysis of the data.

- Prepared manuscript for submission to journal.

Signed: _____ **Date: 06/09/13**

Signed: _____ **Date: 06/09/13**

Signed: _____ **Date: 06/09/13**

8.1 Abstract

Aim: Many people consume alcoholic beverages following a period of physical activity that results in fluid loss through sweating (e.g. after sport, work). Adequate rehydration following physical activity may not occur, consequently resulting in the consumption of alcohol in a dehydrated state. This may have serious implications for the safety of individuals operating motor vehicles. Therefore, this study investigated the impact of mild-moderate dehydration in combination with moderate alcohol consumption on simulated driving performance. **Methods:** Fourteen healthy males participated in a placebo-controlled cross-over design study involving four experimental trials (separated by ≥4days). In each trial, participants were dehydrated by ~2% body mass through exercise. After a 30 min recovery, participants completed a 15 min computerised simulated driving task (Drive 1). In two of the trials, participants were provided with water equivalent to either 50% or 150% body mass loss and also received salt capsules (NaCl, 50mmol/L). A set volume of alcohol or placebo was then consumed in each trial, incorporating the conditions: dehydration-placebo (DP), dehydration-alcohol (DA), partial rehydration-alcohol (PA), and full rehydration-alcohol (FA). The volume of the alcoholic beverage was individually calculated and intended to raise BAC to ~0.05%. The same driving task was then re-administered (Drive 2). Primary outcome measures of driving consisted of standard deviation of lateral position (SDLP), number of side and centre line crossings (LC), number of failures to stop at red traffic signals (FTS), number of impacts/collisions with other vehicles or objects (IMP), and time to collision with a specified lead vehicle (TTC). In addition, reaction time (RT) and incorrect inhibition response (IIR) behaviour to critical events were collected throughout each experimental drive.Subjective ratings of mood and estimates of alcohol intoxication and driving impairment were also recorded in each trial. **Results:** No effects of trial condition were observed on any of the driving performance measures or on subjective ratings of mood, alcohol intoxication, and driving impairment. Standard deviation of lateral position (SDLP) was higher following the consumption of alcohol compared to the placebo trial. However, no differences in SDLP were recorded between the alcohol trials, indicating that hydration level had no observable interaction with alcohol to influence SDLP performance. **Conclusions:** Overall, it appears that dehydration does not exacerbate impairment in driving performance caused by mild-moderate alcohol intoxication. Further research is required to clarify the effects of alcohol and dehydration at various alcohol doses.

8.2 Introduction

The detrimental effects of acute alcohol consumption on driving performance and associated automobile related accidents have been well documented (Moskowitz & Fiorentino, 2000; Connor et al., 2004; Blomberg et al., 2005). Alcohol impairs judgement and physical abilities on discrete tasks related to driving (Ogden & Moskowitz, 2004) as well as actual driving performance (Moskowitz & Robinson, 1988; Moskowitz & Fiorentino, 2000). Whilst there is some evidence that alcohol induced impairment begins at very low alcohol concentrations of 0.01-0.02% (Moskowitz & Burns, 1990; Ogden & Moskowitz, 2004), others suggest a threshold of 0.05% exists for alcohol related impairment (Mitchell, 1985). Evidence from these studies has contributed to the development and application of blood alcohol limits for driving.

Using computer-based driving simulators, moderate doses of alcohol (≥0.05% blood alcohol concentration (BAC)) have been associated with increased driving errors; including greater deviation in lateral position, more lane boundary line crossings, greater rate of steering wheel

movement (Harrison & Fillmore, 2005; Fillmore et al., 2008; Marczinski et al., 2008; Helland et al., 2013), greater deviation in driving speed and acceleration (Quillian et al., 1999; Fillmore et al., 2008; Marczinski et al., 2008), prolonged reaction times to perform tasks (West et al., 1993; Liguori et al., 1999), increased stopping failures to red traffic signals (Fillmore et al., 2008) and more driving related accidents (Marczinski et al., 2008; Creaser et al., 2011). High transferability has been reported between behaviours observed on driving simulators and actual road based vehicles (Lee et al., 2003; Bedard et al., 2010; Mullen et al., 2011). However, external validity is specific to the driving simulator and test scenarios employed. Whilst simulator validation is not always performed, studies that have employed validated driving simulators have demonstrated the important safety implications alcohol consumption has on driving performance, crash risk and driving-related fatalities (Creaser et al., 2011; Mullen et al., 2011).

Adequate hydration is important to human health and cognitive function (Grandjean & Grandjean, 2007; Lieberman, 2010). Performance on discrete cognitive tasks relevant to driving (e.g. attention, reaction time) has been shown to be negatively influenced by acute dehydration (Secher & Ritz, 2012). Reductions in cognitive performance are often observed with fluid deficits at or above 2% body mass loss (Lieberman, 2007; Shirreffs, 2009), with performance deteriorations comparable to those observed following alcohol consumption (Kenefick & Sawka, 2007). Following consumption, alcohol is quickly distributed throughout the water content of the body. Given the overlap in proposed mechanistic actions on the central nervous system such as changes in neurotransmitter actions and altered blood flow (Volkow et al., 1988; Watson & Little, 2002; Wilson & Morley, 2003; Kempton et al., 2009; Kempton et al., 2011), the effects of alcohol under dehydrated conditions may be amplified resulting in greater deterioration of cognitive function. Many people consume alcoholic beverages following a period of physical activity (e.g. after sport and work). In Research Study One (Chapter Five) we observed that population groups such as industrial workers are often challenged by hydration issues and may consume alcohol after work.

This may have serious consequences for the safety of these individuals operating motor vehicles following physical exertion and subsequent alcohol consumption.

In Research Study Three (Chapter Seven), the effects of dehydration, moderate alcohol consumption and rehydration on a range of discrete cognitive functions from the CANTAB were assessed. Alcohol consumption caused deterioration of choice reaction time, executive function and response inhibition, with greater performance decrements observed when participants were dehydrated compared to fully rehydrated. The findings suggest that adequate rehydration following exercise induced fluid loss can attenuate alcohol-related deteriorations in cognitive function. However, to date the combined effects of dehydration and moderate alcohol consumption on simulations of real-world performance, such as driving, are lacking. Therefore, the aim of this study was to investigate if mild or moderate dehydration combined with moderate alcohol consumption causes greater impairment in simulated driving performance compared to the consumption of alcohol under fully rehydrated conditions following exercise. It was hypothesised that the alcohol induced effects on driving performance would be greater when participants were dehydrated compared to trials where they were partially or fully rehydrated.

8.3 Materials and Methods

Participants

Fourteen healthy males (23.6±5.9 yrs, 74.34±10.48 kg BW, 177.9±6.4 cm; (mean±SD)) volunteered to participate in this study. The number of participants was selected following a sample size calculation for one typically assessed driving outcome measure (standard deviation of lateral position, SDLP) using G*Power Version 3.1.7 software. The results of Marczinski et al., (2008) indicated SDLP differences between placebo (1.2±0.4 ft) and alcohol (1.9±0.9 ft) conditions in non-binge drinkers had an effect size of 0.9. To be conservative, we anticipated an effect size of 0.8 and with a power (1-β) of 0.8 and α=0.05 the prediction calculated a sample size of 12

participants was required. Fourteen subjects were recruited to accommodate some attrition due to the experimental burden. Volunteers were recruited via information posters placed around the university campus, with eligibility criteria stipulating that they were male, aged between 18 and 44 yrs, and had a current Australian driving license. Participants had a regular history of alcohol consumption of 5.2±3.7 yrs. The self-reported intake of alcoholic beverages was equivalent to 5.5±3.0 standard drinks (based on the consumption of alcohol from a range of sources including beer, wine and spirits that contain 10g of ethanol) and drinking frequency was reported as 1.2±1.5 times per week using the personal drinking history questionnaire (Vogel-Sprott, 1992). All participants were fully informed of the nature and possible risks of the study before providing written informed consent. The investigation was approved by Griffith University's Human Research Ethics Committee (PBH/25/11/HREC) and the procedures were conducted in accordance with the principles outlined by the agreement of Helsinki.

Preliminary Testing

Each participant visited the laboratory on five occasions. The first visit involved preliminary screening and a familiarisation with the driving simulator and procedures of the study. Participants completed a medical screening questionnaire that provided information on demographics, drinking habits, drug use and physical and mental health status. Individuals with a self-reported psychiatric disorder, head trauma or other CNS injury were excluded from the study. Individuals were also excluded if their responses to the screening questionnaire indicated current drug use, including the use of recreational drugs and psychoactive medications (e.g. benzodiazepines). As an additional screen for alcohol dependence, volunteers with a score of five or higher on the S-MAST (Selzer et al., 1975) were also excluded from the study. Eligible participants then performed two familiarisation drives on the driving simulator using a similar scenario to those employed in the experimental drives, in order to minimise the impact of possible learning effects.

Experimental Design

Each participant undertook four experimental trials (Fig. 8a). The four experimental treatments were randomised via an incomplete Latin square design.
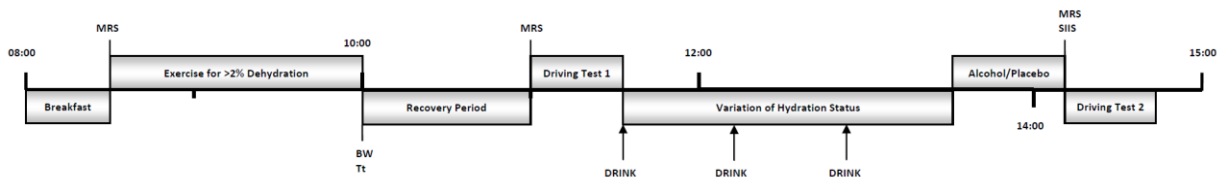

Fig. 8a. Experimental protocol design. Each participant underwent four experimental sessions. Driving Test 1 and 2 correspond to the two simulated driving performance assessments. MRS refers to administration of the mood rating VAS and SIIS refers to the administration of the subjective intoxication and impairment VAS. Drink corresponds to rehydration trials where 50% (P, partial) or 150% (F, full) of fluid loss is replaced.

Pre-Experimental Procedures

Experimental trials were separated by at least four days and were conducted at the same time of the day under similar environmental conditions (25±2°C, 70-80% relative humidity). Participants were asked to refrain from using recreational drugs and non-prescriptive medications for the duration of the study, abstain from alcohol for 24hrs and caffeine-containing substances and moderate-strenuous exercise for 12hrs prior to each experimental trial. During the 24hr period immediately preceding the first trial, participants recorded all food and beverages consumed as well as any exercise completed. A food and exercise record with this information was supplied to each participant and they were asked to repeat this on the day prior to all subsequent trials. Compliance to the pre-experimental procedures was verbally confirmed by participants on arrival to the laboratory. On the morning of each trial, participants were provided with a standardised meal for breakfast (Energy = 25.2±3.8 KJ/Kg BW, CHO = 0.9±0.1 g/Kg BW, Fat = 0.2±0.0 g/Kg BW) which included a breakfast bar (Sanitarium one square meal, Australian Health & Nutrition Ltd.) and 200ml of apple juice (Just Juice, LD&D Australia Pty Ltd.). All dietary preparation and analysis was performed using Foodworks$^{©}$ Version 6.0, 2009, (Xyris Software, Australia) dietary analysis software.

Experimental Procedures

Participants arrived at the laboratory fasted at ~07:00-08:00hrs. Compliance to pre-experimental conditions was verbally acknowledged on arrival before a urine sample was collected to calculate urine specific gravity (U_{sg}) as an initial measure of hydration status. Participants who recorded a U_{sg} reading >1.02, indicating some level of pre-existing hypo-hydration were provided with additional water until a urinary sample fell below the accepted threshold. Five participants required water (500-750ml) on a total of seven occasions. Baseline measures of breath alcohol concentration (BrAC) and tympanic temperature (T_t; Braun ThermoScan®, Welch Allyn) were taken and a baseline blood glucose (BGL) measure was recorded using a finger prick sample (Accuchek Advantage II®, Roche) before participants were provided with the standardised breakfast to consume in 30 min. Immediately following breakfast, participants completed a subjective mood rating scale (MRS) questionnaire (Bond & Lader, 1974) using a computerised visual analogue scale (Marsh-Richard et al., 2009). Participants were then asked to void their bladder completely and an initial nude body weight was measured.

After the body weight measurement, dehydration was induced by intermittent exercise on a cycle ergometer (Monark, Ergomedic 828E, Vansbro, Sweden) at an intensity corresponding to 70-80% of age predicted maximum heart rate (220bpm - age). Details of the dehydration protocol have been outlined in Research Study Two (Chapter Six). After a period of recovery from the exercise protocol, a computerised driving simulation task was used to measure driving performance (Drive 1), which lasted for ~15 min. On completion of the driving test participants were either provided with no water (D), a small amount of water equivalent to 50% body mass loss (P) or a large amount of water equivalent to 150% body mass loss (F), consumed over a two hour time period. In addition, participants received 50mmol/L of sodium (given as NaCl capsules) in trials where water was consumed. Nude body weight was recorded each hour during the rehydration stage for all trials. Immediately prior to providing measures of nude body weight,

participants were asked to void any urine, which was collected in containers and subsequently weighed to calculate cumulative urine loss.

Following the rehydration phase, participants consumed a beverage containing alcohol (A) or placebo (P) to incorporate four experimental conditions: dehydration-placebo (DP), dehydration-alcohol (DA), partial rehydration-alcohol (PA) and full rehydration-alcohol (FA). Alcohol was administered as vodka (Vodka O®, 37% v/v ethanol) made up with equal parts of non-alcoholic ginger beer cordial concentrate (Bickfords®, Australia) and diet ginger beer soft drink (Bundaberg Brewed Drinks Pty Ltd®) and one tenth the volume of lime cordial (Bickfords®, Australia). The volume of the alcoholic beverage was individually calculated and intended to raise BAC to ~0.05% (Watson, et al., 1981). In Australia, the legal blood alcohol limit for the operation of a motor vehicle is 0.05%. The placebo beverage was identical to the alcoholic drink, however water was substituted for vodka. Details of the placebo beverage have been described in Pilot Study One (Chapter 4.2). Participants were not informed of a placebo trial and expected to receive alcohol in all trials. The drink was consumed at a steady pace over 10 min. At the time of drinking the beverage, participants were asked to complete a tasting questionnaire as a measure of expectancy manipulation. The questionnaire has been described in detail in Pilot Study One (Chapter 4.2).

Breath alcohol concentrations (BrAC) were analysed using a police grade Alcolizer LE breathalyser (Alcolizer Pty Ltd) with measurements taken 15 min and 30 min post ingestion. All breathalyser measurements were taken in duplicate, with a triplicate measure recorded if readings differed by ≥0.005%. The measures were averaged to provide the final assessment of BrAC. Participants were not informed of their BrAC measures until after completion of the entire study. Just prior to the 30 min breathalyser, a final MRS and a subjective impairment and intoxication scale (SIIS) were completed using computerised VAS questionnaires. A final BGL was also taken at this time. Immediately after the 30 min breathalyser, a second computerised driving

simulation test was completed (Drive 2) before a final BrAC, urine volume and body weight was recorded (~45 min post ingestion).

Driving Simulator

A computerised driving simulation task was used to measure driving performance (SCANeR studio simulation engine – v1.2r95, OKTAL, Paris, France). The driving simulator was a fixed based model with original controls (accelerator and brake pedals, steering wheel, seat, safety belt, indicator, automatic gear shift and hand brake) from a Hyundai Getz linked to dedicated graphics computer equipment. Visual images were displayed on three 32-inch LCD monitors using three channels, set to provide a 100° front field of view (Fig. 8b). A rear scene was displayed using a single channel on the central monitor to provide images associated with that produced by a typical car rear view mirror. Images from the simulation software were refreshed at a rate of 60Hz, with data sampled at a rate of 20Hz. Auditory and haptic feedback were provided using a stereo sound system and force feedback steering. The simulator also produced vibrations through the driving seat from a four channel sound system to provide a sense of motion. During each of the simulated driving tests, kinematic and behavioural data of the controlled vehicle was recorded by the simulator's software program, which included measures of lateral position, speed, pedal use, and steering wheel movements. SCANeR studio simulator software is equipped with an analysis module allowing recordings of each drive to be collected, which can subsequently be replayed as a video file to view the entire driving scenario or converted to a spreadsheet data set allowing analysis of mathematical determinants from the vehicle model.

Fig. 8b. Computerised driving simulator setup. Fixed base system with original vehicle equipment controls and the visual screen appearance.

The simulated vehicle used automatic transmission and for each drive participants were instructed to stay in the centre of the left-hand lane (traditional for Australian motorists) and adhere to all normal road rules and speed signs. A GPS included in the scenarios provided audio and visual directions (arrow) for the itinerary participants were required to follow. Crashes into other vehicles resulted in the program being reset, with the driver placed in the centre of the left lane at the point of the crash and then allowed to resume the driving task. Because simulator sickness is often an issue in driving simulator studies (Brooks et al., 2010), participants were instructed prior to each drive if they experienced any symptoms of sickness whilst driving the simulator, to immediately cease driving and inform the researcher of their condition.

Experimental Drives

Participants drove an itinerary defined course of 10km, which required approximately 15 min to complete. A detailed description of the driving scenario and performance measures has been outlined in Pilot Study Four (Chapter 4.5). With the exception of average speed and standard deviation of steering angle (SDSA), all other driving performance measures described in Pilot Study Four (Chapter 4.5) were recorded. To reduce the predictability of critical events included in the experimental drives, four parallel scenarios were used, with the events occurring in different

sections of the driving task for each version. In addition, the four parallel versions of the driving test scenario were randomly assigned to the trials for each participant.

The experimental drives were intended to assess naturalistic driving performance, with the exception of reaction time and response inhibition tasks, in order to increase the application of the investigation to real-world driving. As such, participants were given minimal instructions on how to drive during the scenarios, and were provided no task priorities, incentives or performance feedback.

Subjective Ratings

Adaptive Visual Analogue Scales were used to assess mood (Bond & Lader, 1974) and subjective ratings of intoxication and impairment (Fillmore, 2001; Harrison et al., 2007). These scales have been described in detail in Research Study Three (Chapter Seven). In addition to the two driving-related questions used previously, an additional question was included in this study to ascertain "How willing are you to drive a car a short distance (less than 5km) at this time?"

Statistical Analysis

All statistical procedures were performed using SPSS for Windows, Version 21.0 (SPSS Inc., Chicago, IL). All measures were examined for normality and outliers. Planned comparisons were performed to test our specific hypothesis that alcohol induced effects on driving performance parameters would be greater when participants were dehydrated compared to those observed during rehydration trials. In this case, statistical analysis for each of the main dependent variables on the driving task were conducted using paired samples *t*-tests to compare Drive 1 and Drive 2 for each trial where data were normally distributed. On the non-normally distributed data, differences between driving tests were explored with the Wilcoxon matched pairs signed rank test. Comparisons between trials were conducted using one-way repeated-measures analysis of

variance (ANOVA) for normally distributed data and pairwise comparisons were performed where significant main effects were present. On the non-normally distributed data, Friedman's tests were performed to compare observations between trials and contrasts were explored with the Wilcoxon signed rank test. Scores derived from the MRS were subjected to a two-way ANOVA; Protocol (DP, DA, PA, FA) x Time (first, second, third), with both as repeated measures factors. Post hoc analysis was performed on all significant F ratios ($p<0.05$). All other measures (comparisons between trials and across time for BrAC, physiological measures, level of hydration and body mass changes) were analysed by one-way repeated-measures ANOVA and pairwise comparisons were performed where significant main effects were present. For all analyses, when main effects were obtained that required post hoc analysis, least significant difference (LSD) tests were used. When interactions were obtained, paired sample t-tests were used, applying the Bonferroni correction for multiple comparisons. Statistical significance was accepted at $p<0.05$. All data are reported as mean±standard deviation.

8.4 Results

Trial Drink Ratings

Under all trial conditions participants rated the beverage as having alcohol, indicating that the placebo beverage was effective in establishing a belief that alcohol had been received. There was no difference in certainty of perception between the trials, with participants' reporting mean certainty ratings between 'somewhat' and 'very' certain under all conditions. Only one participant was able to correctly identify the placebo beverage as having no alcohol at the time of drinking. This participant was only 'somewhat certain' in their perception.

Driving Performance Measures

All participants completed the experimental drives with no complications or simulator sickness reported. The performance of the 14 participants in the four experimental conditions are summarised in Table 8a. A significant increase in SDLP was observed between driving tests (Drive 1 *vs.* Drive 2) for all alcohol trials (DA, PA, FA; $p<0.05$), with no difference noted between the drives for the placebo trial (DP; $p>0.05$). Mean reaction time to critical events and TTC increased in the DA trial after receiving alcohol and decreased in all other trials after consuming the beverage, however these differences were not significant ($p>0.05$). No other differences in measures of driving performance between experimental drives for each of the trials were observed.

Off road and other vehicle impacts were infrequent in this driving scenario. One participant recorded two impacts during Drive 1 of the PA trial, and one impact in Drive 2 of both the DP and FA trials. Two other participants recorded an impact each, one being in Drive 2 of the DP trial and one being in Drive 1 of the FA trial. The infrequency and low number of overall impact events throughout the study precluded statistical analyses for this performance measure.

Table 8a. Performance measures for experimental drives and change in performance (**Δ**) under each of the trial conditions

	DP			DA			PA			FA		
	Drive 1	Drive 2	Δ	Drive 1	Drive 2	Δ	Drive 1	Drive 2	Δ	Drive 1	Drive 2	Δ
SDLP (cm)	29.1 (5.54)	28.6 (4.28)	-0.5	28.2 (6.41)	30.5 (5.93) *	+2.3	27.6 (6.57)	30.5 (7.69) *	+2.9	26.9 (4.70)	29.5 (5.78) *	+2.6
RT (ms)	1083 (153)	1071 (123)	-12	1062 (162)	1089 (186)	+27	1081 (194)	1061 (166)	-20	1083 (192)	1074 (123)	-9
LC (n)	16.6 (5.13)	15.4 (5.79)	-1.2	13.6 (7.02)	15.6 (6.60)	+2.0	14.4 (7.30)	15.7 (7.68)	+1.3	12.2 (4.79)	15.5 (8.50)	+3.3
TTC (s)	3.57 (2.17)	3.09 (1.63)	-0.48	3.14 (2.17)	3.35 (2.18)	+0.21	2.87 (1.07)	2.49 (1.47)	-0.38	2.87 (1.34)	2.77 (1.08)	-0.10
FTS (n)	0.29 (0.47)	0.29 (0.47)	0	0.00 (0.00)	0.21 (0.43)	+0.21	0.36 (0.63)	0.21 (0.58)	-0.15	0.29 (0.61)	0.57 (0.76)	+0.28
IIR (n)	2.29 (1.68)	1.93 (2.17)	-0.36	1.43 (1.87)	1.36 (2.02)	-0.07	1.36 (1.50)	1.36 (1.74)	0	1.00 (1.57)	1.57 (1.65)	+0.57

DP, dehydration-placebo trial; DA, dehydration-alcohol trial; PA, partial rehydration-alcohol trial; FA, full rehydration-alcohol trial. SDLP = standard deviation of lane position, RT = reaction time to critical events, LC = number of centre and side line crossings, TTC = time to collision with lead vehicle, FTS = number of failures to stop at red lights and stop signs, IIR = number of incorrect inhibition responses to response inhibition critical events. *Significant difference compared to Drive 1 measures (p<0.05). Values are mean (SD).

Mood Ratings

Table 8b shows the results of ANOVA analysis from the MRS questionnaires. A significant main effect for time was observed on all MRS scales and a significant protocol x time interaction was found for the well coordinated-clumsy scale ($p<0.05$). No significant main effect for protocol was found on any of the scales ($p>0.05$). Post hoc analysis revealed higher ratings of drowsiness at time three (Drive 2) compared to time one (beginning of trial) for all trials ($p<0.05$). For the confused-clear headed scale, higher ratings of confusion were observed at time three (Drive 2) compared to previous measures for all trials ($p<0.05$). On the well coordinated-clumsy scale, higher levels of clumsiness were observed at time three (Drive 2) compared to previous times for all alcohol trials, and higher levels of clumsiness at time three compared to time one for the placebo trial ($p<0.05$). For the incompetent-competent scale, higher levels of incompetence were reported at time two (Drive 1) and three (Drive 2) compared to time one for all trials ($p<0.05$). For the lethargic-energetic scale, participants were less energetic at both time three and time two compared to time one ($p<0.05$), but there was no difference in ratings between the two driving times (time two and three, $p>0.05$), indicating that participants' driving performance measures were most likely not influenced by fatigue.

Table 8b. Subjective mood rating scale ANOVA results

Scale	ANOVA		
	Protocol F(3,39)	Time F(2,26)	Protocol x Time Interaction F(6,78)
Alert-Drowsy	0.76	6.47 *	1.12
Confused-Clear Headed	0.45	11.47 *	1.01
Well Coordinated-Clumsy	0.35	26.87 *	3.20 *
Incompetent-Competent	0.53	16.33 *	0.71
Lethargic-Energetic	0.47	8.96 *	0.64

* Significant main or interaction effect ($p<0.05$).

Subjective Intoxication and Perceived Ability to Drive

Participants' subjective ratings of alcohol effects and level of impairment were not different between the three alcohol trials. Ratings for the placebo trial were significantly lower than alcohol trials ($p<0.05$), however there was still some indication of alcohol effects and impairment reported for the placebo trial with mean values on these scales greater than zero. Participants reported that they were less able and less willing to drive a car following alcohol consumption compared to placebo, irrespective of hydration status ($p<0.05$).

Levels of Hydration and Body Mass Changes

The exercise protocol was successful in achieving similar levels of dehydration between trials (Table 8c). Significant differences in percentage of body mass loss were recorded between trials after rehydration had occurred ($p<0.05$). These differences remained significant with the final body weight measurement taken after Drive 2 ($p<0.05$).

Table 8c. Mean percentage of body mass loss compared with initial body weight measure and cumulative urine volume for each trial (n=14)

| Trial | Mean percentage of body mass loss/gain (%) | | | Cumulative Urine Volume (ml) |
	Post Exercise	Post Rehydration	Post Drive 2	
DP	-2.20 ± 0.31	-2.52 ± 0.37	-2.13 ± 0.40	166
DA	-2.16 ± 0.30	-2.50 ± 0.39	-2.13 ± 0.38	185
PA	-2.20 ± 0.44	-1.53 ± 0.37 *	-1.52 ± 0.58 *	452 *
FA	-2.21 ± 0.36	+0.06 ± 0.40 *	-0.57 ± 0.52 *	1334 *

DP, dehydration-placebo trial; DA, dehydration-alcohol trial; PA, partial rehydration-alcohol trial; FA, full rehydration-alcohol trial. *Significant difference from all other trials ($p<0.05$). Values are mean ± SD.

Fluid Intake and Urine Volume

Total fluid intake (including alcohol/placebo consumption) was significantly different between the two rehydration trials and between both rehydration and dehydration trials as expected ($p<0.05$). A significantly greater urine output was measured between both rehydration (PA and FA) trials and the dehydration (DP and DA) trials (Table 8c, $p<0.05$). There was also a significant difference in urine output between the two rehydration (PA and FA) trials ($p>0.05$).

Physiological Measures

As expected, tympanic temperature recordings indicated an increase in body temperature following exercise for all trials. Temperature measurements recorded prior to both Drive 1 (~36.5±0.5°C) and Drive 2 (~36.5±0.3°C) were significantly higher than pre-trial (~36.1±0.4°C) measures for all trials ($p<0.05$), however the differences were not considered clinically significant and were generally within the error margins indicated for accuracy of the tympanic device (±0.2°C). Blood glucose responses revealed that participants were never in a hypoglycaemic state when completing the test drives. Values were significantly higher at Drive 1 measures compared to pre-trial measures for the DA and PA trials (~7.1±1.0mmol/L vs. ~6.4±0.9mmol/L, $p<0.05$), but not for the DP and FA trials (~7.1±1.3mmol/L vs. ~6.6±1.3mmol/L, $p>0.05$). Following consumption of the placebo or alcohol beverage blood glucose levels increased significantly in all trials (~10.0±1.4mmol/L, $p<0.05$).

Breath Alcohol Concentrations

No significant difference in BrAC was recorded between alcohol trials at any of the measured time points ($p>0.05$). Breath alcohol concentrations achieved 30 min post alcohol ingestion when participants were required to complete the driving test were 0.045±0.006%, 0.043±0.003% and 0.043±0.006% for the DA, PA and FA trials respectively. As expected, no measurable breath alcohol

was detected for the DP trial (Fig. 8c). The driving test was performed 30 min after drinking and lasted for 15 min. Final BrACs measured at the end of the driving test were not significantly different from pre-driving BrAC levels ($p>0.05$), indicating that the task was performed when alcohol concentrations were relatively stable (0.045±0.005%, 0.044±0.004% and 0.044±0.007% for DA, PA and FA trials respectively on completion of the driving test).
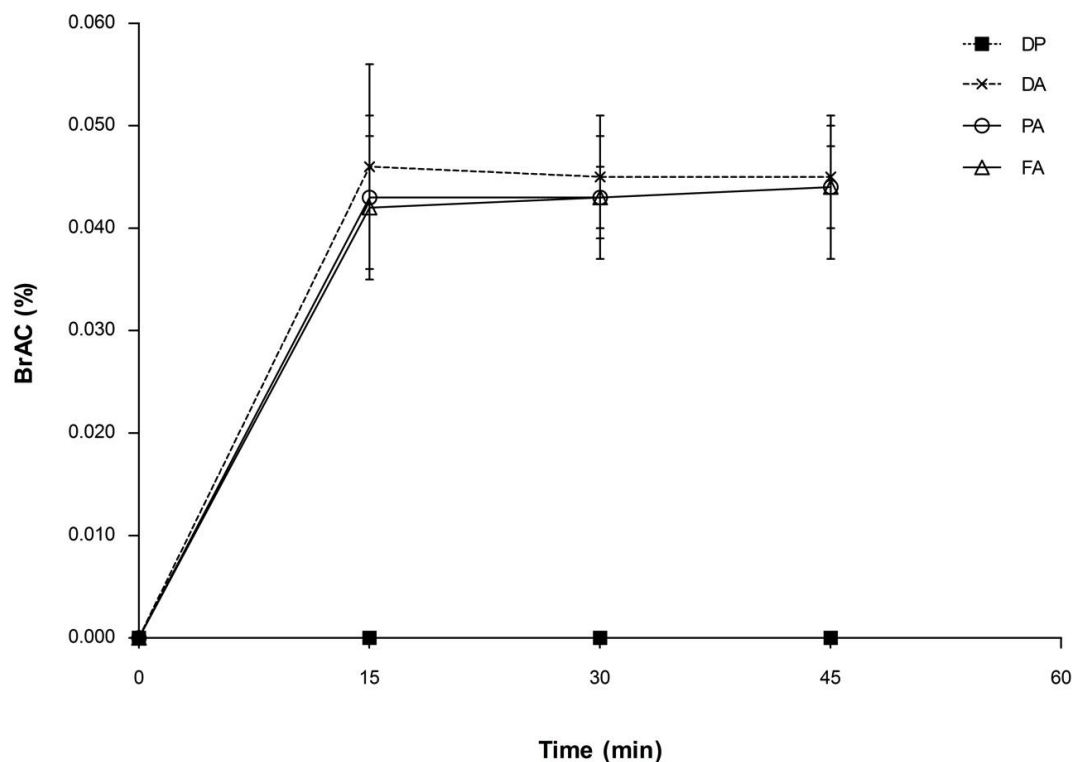
Fig. 8c. Breath alcohol concentration post beverage administration for each trial. DP, dehydration-placebo trial; DA, dehydration-alcohol trial; PA, partial rehydration-alcohol trial; FA, full rehydration-alcohol trial. Values are mean ± SD.

8.5 Discussion

To our knowledge the present investigation is the first to examine the impact of exercise induced dehydration and moderate alcohol consumption on simulated driving performance. Contrary to our hypothesis, no observable interactive effects were found between mild to moderate dehydration and moderate alcohol consumption on individual measures of driving performance. These results suggest that individuals who consume moderate amounts of alcohol

(eliciting a BrAC below 0.05%) following a period of physical activity causing fluid loss are unlikely to experience further impairment in driving related performance than that observed with alcohol alone.

In this study, participants completed a 15 min naturalistic driving task, in which measures of vehicle control (SDLP, LC), violation of driving regulations (FTS), interactive traffic behaviour (IMP, TTC) and other associated discrete tasks (RT, IIR) were assessed throughout. On measures of vehicle control, no observable effects of alcohol combined with various levels of hydration status were detected. Standard deviation of lateral position was higher following the consumption of alcohol irrespective of hydration status. However, in the placebo trial SDLP between driving tests was unchanged. These results support the findings of previous work in which a moderate dose of alcohol (~0.04%) has been shown to have a significantly positive correlation with SDLP (Helland et al., 2013). The absolute values in SDLP were also similar for both the placebo and alcohol conditions to those observed in previous driving simulator studies (Mets et al., 2011; Helland et al., 2013). Collectively, these results suggest that a moderate dose of alcohol (inducing BrACs between 0.04-0.05%) increases deviation in lane position. Standard deviation of lane position is regarded as a potential index of driving safety (Verster & Roth, 2011) and increases in SDLP could potentially lead to lane crossings into adjacent traffic lanes or the road shoulder that may have severe consequences. However, one could argue that the magnitude of change observed following alcohol consumption in the present study (~2-3cm) may not have meaningful relevance in terms of traffic safety. Verster and Roth (2011) suggest a clinically relevant cut-off point of impairment for SDLP is important, with studies often using +2.4cm at alcohol concentrations of 0.05% as comparative data. However these results refer to the standardised Dutch on-road driving test and Helland et al. (2013) observed considerably higher SDLP values in simulated driving compared to real driving using identical test scenarios. In addition, Helland et al. (2013) reported higher BAC-related increases in SDLP in simulated driving compared to real driving. Thus, whilst significant

increases in SDLP were observed following alcohol consumption in the present study, these results may not directly translate to increases in real driving related accident risk.

Similar results were observed for number of line crossings during the driving tests. Whilst results were not statistically significant, the number of line crossings increased following the consumption of alcohol under all hydration conditions but was reduced in the placebo trial when directly compared to the initial driving tests. Previous work has reported more roadway departures and a higher number of centre and side line crossings following the consumption of moderate alcohol doses (Arnedt et al., 2001; Fillmore et al., 2008). However, in these studies blood alcohol concentrations were higher than those in the current study (0.055-0.086%), which may explain the more definitive results observed. Absolute values for the number of line crossings were also much higher in the present study compared to previous studies. The relatively demanding driving scenario that was used in our experiment may account for these differences. Participants were required to complete a number of left and right hand turns during the drive, which may have led to more over and under steering, thus increasing the chances of deviating outside the driving lane and recording a line crossing. Taken together, this indicates that alcohol consumption is likely to increase the number of line crossings, but the magnitude of any such increase may be dependent on the volume of alcohol consumed and the difficulty of the driving task.

No interactive effects between alcohol and hydration status were observed for violations of driving regulations and interactive traffic behaviour measures in this study. Guidelines for the safe driving of motor vehicles in Australia indicate that individuals should not drive closer than two to three seconds from the vehicle ahead in good driving conditions (Transport: Roads and Maritime Services, 2012). No significant differences in TTC between the different trial conditions were observed and participants drove within the recommended guidelines for safe following behaviour under all trial conditions, indicating that participants were able to apply safe car following

techniques regardless of hydration status or alcohol intoxication. Number of stopping failures was not different between drives for all trial conditions. Given that very few stopping failures were made under all trial conditions it is possible that decision errors or misjudgements by participants (they thought they could clear the intersection before the red light but failed) explain these results. An increase in stopping failures has been observed after alcohol consumption in previous work (Fillmore et al., 2008), however alcohol doses were considerably higher (~0.08%) than observed in the present study. Further investigation of hydration conditions with higher doses of alcohol on this driving performance measure is required.

Performance on discrete tasks such as reaction time and response inhibition critical events was not influenced by alcohol and hydration status in this study. In Research Study Three (Chapter Seven), choice reaction time and response inhibition performance was adversely affected when alcohol was consumed under dehydrated conditions, yet unaffected when adequate rehydration occurred prior to the consumption of alcohol. Whilst no significant differences were observed in this study, interestingly, a small increase in reaction time was seen following alcohol consumption on the DA trial and small decreases were observed in all other trials. In Research Study Three (Chapter Seven), choice reaction time was assessed using an isolated task on the CANTAB instrument and alcohol intoxication levels were slightly higher during the performance task (~0.06%). The critical event task in the present study was more typical of a simple reaction time task, although the overall task demands may have been higher given that participants were required to perform the reaction tasks whilst driving. It is possible that the intoxication level attained in this study was not high enough to influence performance on these tasks. Alternatively, the critical events employed may not have been sensitive enough to detect significant changes between trial conditions.

Overall, the results of this study indicate that dehydration through sweat loss in combination with moderate alcohol consumption (to levels permissible with legal driving laws of Australia) does

not influence measures of driving performance. However, these results may not be replicated at higher alcohol concentrations. Given that legal alcohol limits for driving are higher in other countries (e.g. 0.08% in the USA), and results from Research Study Three (Chapter Seven) indicate effects on cognitive performance at slightly higher alcohol intoxication levels, it may be important to explore the effects of these conditions on driving performance with different doses of alcohol.

Hydration level did not have any effect on BrAC measures in this study. Similar results were reported in Research Studies Two and Three (Chapters Six and Seven respectively). Interestingly, however, whilst identical alcohol doses were used between studies, peak BACs achieved in the present study were lower than those observed in Research Study Three (Chapter Seven; ~0.04% vs. ~0.06% respectively). An explanation for this is likely due to the differences in carbohydrate content of the alcohol containing beverage. Manufacturers for the ginger beer cordial concentrate used in the previous study no longer produce a sugar-free product. Thus for the current study we were required to use a regular sugar sweetened ginger beer mixer. Recent work by Marczinksi and Stamates (2013) support these findings, reporting elevated BrACs when alcohol was mixed with a diet soft drink compared with the same amount of alcohol mixed with sugar-sweetened beverage.

Alcohol and dehydration have independently been associated with a deterioration in mood state (Lex et al., 1988; Heishman et al., 1997; Lieberman, 2007; Shirreffs, 2009). Human factors such as emotion and mood are likely to influence behaviours such as aggressive driving, thereby attributing to factors that cause traffic accidents (Matthews et al., 2011; Moller, 2011; Hu et al., 2013). In Research Studies Two and Three (Chapters Six and Seven respectively), no effect of combined alcohol and dehydration conditions on subjective ratings of mood were observed. Similarly, in this study no effect of trial condition was observed on subjective ratings of mood, indicating that hydration level had no observable impact on mood state when alcohol was consumed. Participants' rating of clumsiness was increased after the consumption of alcohol regardless of hydration status, which may suggest that the effects of alcohol outweigh the effects

of dehydration on some subjective states. However, overall the results of this study suggest that subjective perceptions of effects from the different trial conditions were not instrumental in the inability to detect observable changes in driving performance.

One of the limitations of the current study is that the study design did not include placebo protocols for the partial rehydration and full rehydration trials. It is therefore difficult to make accurate conclusions about the relative effects of hydration and alcohol on driving performance because the effects of alcohol and level of dehydration cannot be readily separated. Whilst it was not the intention of this study to investigate dose response effects, incorporation of a placebo arm under different hydration conditions may provide greater insight into the effects of these conditions. A limited sample size was also employed in this study, which may reduce the power of the results. However, due to the considerable time requirement and burden placed on participants, in addition to the exhaustion of resources, a larger sample size was not possible. The use of a repeated measures study design was employed to assist with statistical power and reduces the variance of estimates of treatment effects. This study also involved a naturalistic driving scenario, however, measures of reaction time and response inhibition were assessed throughout drives using discrete tasks that were hardly naturalistic. The use of these elements may not reflect performance in the real world, thus reducing the ecological validity of some results. Finally, studies comparing performance on this particular simulator with road driving measures have not been conducted. Thus, translation of results from the simulator into real-world driving performance outcomes cannot readily be made. Whilst it was not the intention of this study to compare driving performance to on-road driving and rather compare the effects of hydration and alcohol treatments on changes in simulated driving performance, this remains a limitation of the current study and further research is required.

In summary, this study investigated the impact of mild and moderate dehydration combined with moderate alcohol consumption on measures of simulated driving performance. Results found

no overall difference in driving performance between trial conditions and it appears that dehydration does not seem to have an effect in exacerbating impairment in driving performance caused by alcohol intoxication. However, alcohol doses used in this study produced intoxication levels (0.04%) slightly below the legal driving limit for Australian motorists (0.05%). Further research is required to clarify and establish the effects of alcohol and dehydration at different alcohol doses.

Chapter Nine: Conclusion

9.1 Overview of Findings

The overall aim of this thesis was to examine the combined effects of mild to moderate dehydration and moderate alcohol consumption on human behaviour and performance, with specific emphasis given to discrete cognitive functions associated with driving a motor vehicle and actual driving performance itself. A review of the thesis aims and main findings of each research study are outlined in Table 9.1.

Table 9.1. Overview of the aims of the thesis and the main findings of each Research Study

Research Study	Research Aims	Main Findings
One	Determine hydration status of industrial workers and explore typical post-work behaviours, attitudes and perceptions relating to alcohol consumption.	1. Approximately one-third of workers were inadequately hydrated either at the beginning or end of work shifts. 2. Most of the workers believed alcohol consumption after work was acceptable, and a lack of consideration for hydration levels was indicated prior to consuming alcohol.
Two	Examine the effects of exercise-induced dehydration on alcohol pharmacokinetics and subjective ratings of alcohol's effects.	1. Dehydration had no impact on the pharmacokinetic response to a moderate dose of alcohol. 2. Participants' subjective ratings of confusion and level of intoxication were lower when alcohol was consumed in dehydrated conditions, indicating that they felt less confused and less intoxicated under these conditions. 3. Dehydration may influence risk taking behaviour, with greater willingness to drive observed in dehydration trials.
Three	Examine the effects of mild to moderate dehydration combined with moderate alcohol consumption on a range of cognitive functions using the CANTAB.	1. Alcohol consumption caused deterioration on some CANTAB measures (i.e. choice reaction time, executive function, response inhibition). 2. Performance impairment was exacerbated when participants were dehydrated. 3. Subjective ratings of impairment and intoxication were not influenced by hydration status.

Table 9.1 *(continued)*

Research Study	Research Aims	Main Findings
Four	Examine the effects of mild to moderate dehydration combined with moderate alcohol consumption on simulated driving performance.	1. No effect of hydration status combined with alcohol consumption was observed on measures of simulated driving performance. 2. Alcohol consumption had some influence on SDLP but there was no observable interaction with hydration status influencing performance. 3. No combined effects of hydration status and alcohol consumption were observed on subjective ratings of mood, alcohol intoxication and driving impairment.

The findings of the four Research Studies and the literature review have been considered as a collective and integrated body of research. In Research Study One, it was hypothesised that some individuals from the work population investigated would indicate levels of dehydration following daily physical exertion and consume alcohol as part of post-work behaviour with little or no regard for their hydration status. Results from the study supported the hypothesis with almost one-third of the workers recording urine analysis measures for inadequate hydration status. Some workers consumed alcohol after work in a dehydrated state. However, more importantly workers perceptions toward alcohol consumption indicated acceptance for the practice with little regard given to hydration status prior to alcohol consumption. This suggests population groups such as industrial workers may be particularly vulnerable to experiencing dehydration in the workplace and participate willingly in post work rehydration practices that involve alcohol consumption. In addition it highlights the importance of understanding the perceptions of this population group with regards to alcohol consumption and the challenges in overcoming workplace culture to promote effective rehydration strategies that improves the overall health and safety of workers.

In Research Study Two, it was hypothesised that alcohol pharmacokinetic variables associated with the blood alcohol curve would be significantly affected by dehydration, leading to higher BAC levels and greater ratings of perceived intoxication effects when alcohol was consumed in a

dehydrated state compared to a euhydrated state. Contrary to our hypothesis, we observed no effect of hydration status on the pharmacokinetic response to alcohol, including no observable increase in peak BAC and BrAC. On the other hand, participants' subjective ratings of confusion and level of intoxication were lower when alcohol was consumed under dehydrated conditions, indicating that they felt less confused and less intoxicated consuming alcohol when dehydrated. In addition, participants had a greater willingness to drive under these conditions. Whilst there was no influence of dehydration on the physiological fate of alcohol in the body, the results suggest that there may be some interactive effect of dehydration and alcohol on the subjective effects of alcohol. This could have direct implications for individuals if they were to consume alcohol in a dehydrated state, have a diminished ability to perceive the effects of alcohol intoxication and engage in risk-taking behaviour (i.e. driving under the influence).

In Research Study Three, it was hypothesised that alcohol-induced effects on cognitive performance would be greater when individuals were dehydrated compared to those observed when rehydrated after exercise. Results from the study supported the hypothesis indicating an interaction between dehydration and alcohol consumption on some cognitive functions (i.e. choice reaction time, executive function, response inhibition), with restoration of fluid losses attenuating the alcohol-induced deterioration. However, in direct contrast to the subjective ratings reported in Research Study Two, subjective ratings of impairment, intoxication and driving-related risk behaviour were not influenced by hydration status in this study. In addition these results suggest that the interaction between dehydration and alcohol does not produce systematic effects uniformly across all tasks or measures of cognitive function.

In Research Study Four, it was hypothesised that alcohol induced effects on measures of driving performance would be greater when individuals were dehydrated compared to those observed when rehydrated following exercise. In contrast to our hypothesis, it appears that dehydration has no observable interactive effect with moderate alcohol consumption on simulated driving

performance. An explanation for the absence of any deterioration in performance observed in this study may relate to the level of alcohol intoxication employed or an inability to detect changes in performance below the sensitivity of the driving simulator measures used.

Overall, it appears that mild to moderate dehydration may exacerbate alcohol induced impairment of some cognitive functions and behaviours. However, the interactive effect of dehydration and alcohol does not appear to be uniform across tasks or influential on performance tasks of an applied nature (i.e. driving performance) at levels below enforceable driving limits in Australia (BAC <0.05%). In a population group likely to experience fluid loss (i.e. industrial workers), little consideration appears to be given to hydration status prior to the consumption of alcohol. Whilst hydration status does not seem to affect the pharmacokinetic response to alcohol, in doses that produce intoxication levels above 0.05%, impairment of discrete cognitive skills may be exacerbated and there may be some influence on the subjective effects of alcohol and associated risk-taking behaviours (i.e. willingness to drive a motor vehicle). This could have serious implications for individuals who consume alcohol in amounts likely to attain intoxication levels above 0.05%, following a period of fluid loss that causes dehydration.

9.2 Implications of the Research

Overall, the research from this thesis has shown that the combined effects of dehydration and moderate alcohol consumption can be detrimental to discrete cognitive functions and may influence decisions involving driving-related risk-taking behaviour.

From a practical standpoint, the research from this thesis indicates that individuals who consume moderate amounts of alcohol following a period of fluid loss causing dehydration, may perform some driving associated cognitive skills poorer than if they were fully rehydrated prior to alcohol consumption. They may also be more likely to engage in driving-related risk-taking behaviour under these conditions than they would otherwise. Whilst no interactive effects were

observed between alcohol and dehydration on driving performance in this body of work, it would not be advisable to dismiss any effect being observed at higher alcohol doses or with more sensitive driving simulator instruments.

In the USA, combined data from the National Highway Traffic Safety Administration's (NHTSA's) 1995 National Survey of Drinking and Driving Attitudes and behaviors (NSDDAB) and FBI crime reports indicate that motorists admit to driving with alcohol impairment in about one in six trips, and to being over the legal limit in about one in nine trips (Zador et al., 2000). Given this level of disregard for enforceable BAC limits, the results from the Research Studies in this thesis may be even more significant. If alcohol-induced impairment in driving-related cognitive skills are exacerbated with dehydration, this may have serious and even fatal consequences for individuals who consume more than permissible levels of alcohol after a period of physical exertion that causes fluid loss and consider driving a motor vehicle.

9.3 Future Considerations

As a result of the research within this thesis, a number of recommendations for further research can be made:

Firstly, results from Research Study Four (Chapter Eight) indicated that dehydration in combination with moderate alcohol consumption did not influence measures of driving performance. However, the levels of intoxication attained in this study were below the legal driving limit for an Australian context (BrAC <0.05%). These findings may not apply at higher alcohol concentrations. Legal alcohol limits for driving are higher in other countries (e.g. 0.08% in the USA). In addition, motorists admit to driving with BACs above the legal limit and results from Research Study Three (Chapter Seven) indicate effects on discrete driving-related cognitive skills at slightly higher alcohol intoxication levels (BrAC >0.05%). Given this evidence, it would be

appropriate to explore the effects of dehydration and alcohol consumption on driving performance with higher doses of alcohol and on high fidelity driving simulators with greater sensitivity to detect changes.

Secondly, in Research Study Two (Chapter Six), subjective ratings of confusion and intoxication level, and willingness to drive a motor vehicle after consuming alcohol were influenced by dehydration, with lower symptoms and more willingness to drive reported when participants were dehydrated compared to euhydrated. However, in Research Studies Three and Four (Chapters Seven and Eight respectively), no effect of hydration level was observed on these same subjective ratings following alcohol consumption. In Research Study Two, the exercise task was only employed for one trial to induce dehydration, with the euhydration trials not requiring exercise to be performed. In the later Research Studies (Research Studies Three and Four), exercise was performed in all trials prior to different rehydration protocols. It is possible that the exercise task in these studies may have affected participants' cognitive function and mood, decreasing their sensitivity to the effects of alcohol and resulting in reduced subjective ratings of confusion and intoxication. An effect may not have been able to be detected in the later studies because exercise was performed in all trials and differences may only exist in comparison to non-exercise euhydration states. Further research into the effects of dehydration with and without an exercise component on subjective ratings of alcohol intoxication, impairment and driving-related risk-taking behaviour is required.

Finally, the context of this research has centred around the influence of dehydration and alcohol consumption on driving related performance and behaviours. As described in Chapter Two of this thesis, alcohol consumption is undoubtedly a significant contributor to many harmful situations. Binge and excessive drinking are serious public health issues in Australia and the wider international community. Risk-taking behaviour that accompanies excessive alcohol consumption is responsible for far too many of the tragic circumstances that are witnessed each year. The role

of hydration status in the decision-making process involving risk-taking behaviours (i.e. drink-driving, anti-social behaviour, violence, drug use) should be investigated on a broader level.

References

Abbey A, Smith M, Scott R. The relationship between reasons for drinking alcohol and alcohol consumption: An interactional approach. *Addictive Behaviors*, 1993; 18(6):p659-670.

Abroms B, Fillmore M, Marczinski C. Alcohol-induced impairment of behavioral control: Effects on the alteration and suppression of prepotent responses. *Journal of Studies on Alcohol*, 2003; 64(5):p687-695.

Ackland G, Harrington J, Downie P, Holding J, Singh-Ranger D, Griva K, Mythen M, Newman S. Dehydration induced by bowel preparation in older adults does not result in cognitive dysfunction. *Anesthesia and Analgesia*, 2008; 106(3):p924-929.

Adam G, Carter R, Cheuvront S, Merullo D, Castellani J, Lieberman H, Sawka M. Hydration effects on cognitive performance during military tasks in temperate and cold environments. *Physiology and Behavior*, 2008; 93(4-5):p748-756.

Ahearn E. The use of visual analog scales in mood disorders: A critical review. *Journal of Psychiatric Research*, 1997; 31(5):p569-579.

Akinwuntan A, Tank R, Vaughn L, Wilburn A, Easton S. Normative values for driving simulation parameters: A pilot study. *Proceedings of the Fifth International Driving Symposium on Human Factors in Driver Assessment, Training and Vehicle Design,* 2009; Big Sky, Montana, p161-168.

Alcohol Education & Rehabilitation Foundation. *Annual alcohol poll: Community attitudes and behaviours*. Deakin, ACT; 2011.

Allen A, Meda S, Skudlarski P, Calhoun V, Astur R, Ruopp K, Pearlson G. Effects of alcohol on performance on a distraction task during simulated driving. *Alcoholism: Clinical and Experimental Research*, 2009; 33(4):p617-625.

Allen R, Rosenthal T, Cook M. *A short history of driving simulation*. In Fisher D, Rizzo M, Caird J, Lee J (Eds.), Handbook of driving simulation for engineering, medicine, and psychology; 2011. Boca Raton, FL: CRC Press.

Allen T, White A. (2010). *Assessment of carbon monoxide exposure and physiological stress at an australian motor sport event*. Paper presented at the Medicine in Motor Sport Summit and CMO Seminar, Valencia, Spain.

Altman D. *Practical statistics for medical research*; 1991. London: Chapman and Hall.

Altman D, Bland J. Measurement in medicine: The analysis of method comparison studies. *Journal of the Royal Statistical Society. Series D (The Statistician)*, 1983; 32(3):p307-317.

Armstrong L. Hydration assessment techniques. *Nutrition Reviews*, 2005; 63(6):p40-54.

Armstrong L. Assessing hydration status: The elusive gold standard. *Journal of the American College of Nutrition*, 2007; 26(5 Suppl):p575-584.

Armstrong L, Ganio M, Casa D, Lee E, McDermott B, Klau J, Jimenez L, Le Bellego L, Chevillotte E, Lieberman H. Mild dehydration affects mood in healthy young women. *Journal of Nutrition*, 2012; 142:p382-388.

Armstrong L, Maresh C, Castellani J, Bergeron M, Kenefick R, LaGasse K, Riebe D. Urinary indices of hydration status. *International Journal of Sport Nutrition*, 1994; 4(3):p265-279.

Armstrong L, Pumerantz A, Fiala K, Roti M, Kavouras S, Casa D, Maresh C. Human hydration indices: Acute and longitudinal reference values. *International Journal of Sport Nutrition and Exercise Metabolism*, 2010; 20(2):p145-153.

Armstrong L, Soto J, Hacker F, Casa D, Kavouras S, Maresh C. Urinary indices during dehydration, exercise, and rehydration. *International Journal of Sport Nutrition*, 1998; 8(4):p345-355.

Arnaud M. *Hydration throughout life*; 1998. London: John Libbey and Company Ltd.

Arnedt J, Wilde G, Munt P, Maclean A. Simulated driving performance following prolonged wakefulness and alcohol consumption: Separate and combined contributions to impairment. *Journal of Sleep Research*, 2000; 9(3):p233-241.

Arnedt J, Wilde G, Munt P, MacLean A. How do prolonged wakefulness and alcohol compare in the decrements they produce on a simulated driving task? *Accident Analysis and Prevention*, 2001; 33(3):p337-344.

Atkinson G, Nevill A. Statistical methods for assessing measurement error (reliability) in variables relevant to sports medicine. *Sports Medicine*, 1998; 26(4):p217-238.

Baker L, Conroy D, Kenney W. Dehydration impairs vigilance-related attention in male basketball players. *Medicine and Science in Sports and Exercise*, 2007; 39(6):p976-983.

Band G, van der Molen M, Logan G. Horse-race model simulations of the stop-signal procedure. *Acta Psychologica*, 2003; 112(2):p105-142.

Bandelow S, Maughan R, Shirreffs S, Ozgunen K, Kurdak S, Ersoz G, Binnet M, Dvorak J. The effects of exercise, heat, cooling and rehydration strategies on cognitive function in football players. *Scandinavian Journal of Medicine & Science in Sports*, 2010; 20(3 Suppl):p148-160.

Banderet L, MacDougall D, Roberts B, Roberts D. *Effects of dehydration or cold exposure and restricted fluid intake upon cognitive performance*. US Army Research Institute of Environmental Medicine, 1984. M38/84.

Banks S, Catcheside P, Lack L, Grunstein R, McEvoy R. Low levels of alcohol impair driving simulator performance and reduce perception of crash risk in partially sleep deprived subjects. *Sleep*, 2004; 27(6):p1063-1067.

Baraona E, Abittan C, Dohmen K, Moretti M, Pozzato G, Chayes Z, Schaefer C, Lieber C. Gender differences in pharmacokinetics of alcohol. *Alcoholism: Clinical and Experimental Research*, 2001; 25(4):p502-507.

Barkley R, O'Connell T, Murphy K, Anderson D, Connor D. Effects of two doses of alcohol on simulator driving performance in adults with attention-deficit/hyperactivity disorder. *Neuropsychology*, 2006; 20(1):p77-87.

225

Bartoli W, Davis J, Pate R, Ward D, Watson P. Weekly variability in total body water using $2h_2o$ dilution in college-age males. *Medicine and Science in Sports and Exercise*, 1993; 25(12):p1422-1428.

Bates G. What are the fluid replacement guidelines for workers. *Australian Journal of Nutrition & Dietetics*, 1996; 53(4 Suppl):p44-46.

Bates G, Miller V. Sweat rate and sodium loss during work in the heat. *Journal of Occupational Medicine and Toxicology*, 2008; 3(4):p4-10.

Bates G, Miller V, Joubert D. Hydration status of expatriate manual workers during summer in the middle east. *Annals of Occupational Hygiene*, 2010; 54(2):p137-143.

Bates G, Parker R, Ashby L, Bentley T. Fluid intake and hydration status of forest workers: A preliminary investigation. *International Journal of Forest Engineering*, 2001; 12(2):p27-32.

Bates G, Schneider J. Hydration status and physiological workload of uae construction workers: A prospective longitudinal observational study. *Journal of Occupational Medicine and Toxicology*, 2008; 3:p21-31.

Bedard M, Parkkari M, Weaver B, Riendeau J, Dahlquist M. Assessment of driving performance using a simulator protocol: Validity and reproducibility. *American Journal of Occupational Therapy*, 2010; 64(2):p336-340.

Beglinger L, Gaydos B, Tangphao-Daniels O, Duff K, Kareken D, Crawford J, Fastenau P, Siemers E. Practice effects and the use of alternate forms in serial neuropsychological testing. *Archives of Clinical Neuropsychology*, 2005; 20(4):p517-529.

Benedict F. The alcohol program of the nutrition laboratory with special reference to psychological effects of moderate doses of alcohol on man. *Science*, 1916; 43(1122):p907-917.

Benelam B, Wyness L. Hydration and health: A review. *Nutrition Bulletin*, 2010; 35(1):p3-25.

Benton D. Dehydration influences mood and cognition: A plausible hypothesis? *Nutrients*, 2011; 3(5):p555-573.

Bernosky-Smith K, Shannon E, Roth A, Liguori A. Alcohol effects on simulated driving in frequent and infrequent binge drinkers. *Human Psychopharmacology*, 2011; 26(3):p216-223.

Berry J, Pidd K, Roche A, Harrison J. Prevalence and patterns of alcohol use in the australian workforce: Findings from the 2001 national drug strategy household survey. *Addiction*, 2007; 102(9):p1399-1410.

Biggs C, Paterson M, Maunder E. Hydration status of south african forestry workers harvesting trees in autumn and winter. *Annals of Occupational Hygiene*, 2011; 55(1):p6-15.

Bird C, Papadopoulou K, Ricciardelli P, Rossor M, Cipolotti L. Test-retest reliability, practice effects and reliable change indices for the recognition memory test. *British Journal of Clinical Psychology*, 2003; 42(4):p407-425.

Bishop P, Pieroni R, Smith J, Constable S. Limitations to heavy work at 21°c of personnel wearing the u.S. Military chemical denfense ensemble. *Aviation, Space, and Environmental Medicine*, 1991; 62(3):p216-220.

Black D, Lawson J, Fleishman S. Excessive alcohol use by non-elite sportsmen. *Drug and Alcohol Review*, 1999; 18(2):p201-205.

Blair S, Jacobs D, Powell K. Relationships between exercise or physical activity and other health behaviors. *Public Health Reports*, 1985; 100(2):p172-180.

Bland J, Altman D. Regression analysis. *Lancet*, 1986a; 1(8486):p908-909.

Bland J, Altman D. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet*, 1986b; 1(8476):p307-310.

Bland J, Altman D. Measuring agreement in method comparison studies. *Statistical Methods in Medical Research*, 1999; 8(2):p135-160.

Blomberg R, Peck R, Moskowitz H, Burns M, Fiorentino D. *Crash risk of alcohol involved driving: A case-control study*. Dunlap & Associates Inc, Stanford; 2005. DTNH22-94-C-05001.

Bogen E. Drunkeness: A quantitative study of acute alcoholic intoxication. *Journal of the American Medical Association*, 1927; 89(18):p1508-1511.

Bond A, Lader M. The use of analogue scales in rating subjective feelings. *British Journal of Medical Psychology*, 1974; 47(3):p211-218.

Brackstone M, Waterson B, McDonald M. Determinants of following headway in congested traffic. *Transportation Research Part F: Traffic Psychology and Behaviour*, 2009; 12(2):p131-142.

Brake D, Bates G. Fluid losses and hydration status of industrial workers under thermal stress working extended shifts. *Occupational and Environmental Medicine*, 2003; 60(2):p90-96.

Brenner J, Swanik K. High-risk drinking characteristics in collegiate athletes. *Journal of American College Health*, 2007; 56(3):p267-272.

Brooks J, Goodenough R, Crisler M, Klein N, Alley R, Koon B, Logan W, Ogle J, Tyrrell R, Wills R. Simulator sickness during driving simulation studies. *Accident Analysis and Prevention*, 2010; 42(3):p788-796.

Browman K, Crabbe J. Alcohol and genetics: New animal models. *Molecular Medicine Today*, 1999; 5(7):p310-318.

Bureau of Meteorology (website). 2012, Retrieved 8 March, 2012; Available from: http://www.bom.gov.au/jsp/ncc/climate_averages

Burian S, Hensberry R, Liguori A. Differential effects of alcohol and alcohol expectancy on risk-taking during simulated driving. *Human Psychopharmacology*, 2003; 18(3):p175-184.

Burian S, Liguori A, Robinson J. Effects of alcohol on risk-taking during simulated driving. *Human Psychopharmacology*, 2002; 17(3):p141-150.

Caird J, Horrey W. *Twelve practical and useful questions about driving simulation*. In Fisher D, Rizzo M, Caird J, Lee J (Eds.), Handbook of driving simulation for engineering, medicine, and psychology; 2011. Boca Raton, FL: CRC Press.

Caldwell J, Engelen L, van der Henst C, Patterson M, Taylor N. The interaction of body armor, low-intensity exercise, and hot-humid conditions on physiological strain and cognitive function. *Military Medicine*, 2011; 176(5):p488-493.

Calhoun V, Pekar J, Pearlson G. Alcohol intoxication effects on simulated driving: Exploring alcohol-dose effects on brain activation using functional mri. *Neuropsychopharmacology*, 2004; 29(11):p2097-2107.

Cambridge Cognition Limited. *Cantabeclipse: Test administration guide*; 2006. Cambridge, UK.

Carmichael F, Israel Y, Crawford M, Minhas K, Saldivia V, Sandrin S, Campisi P, Orrego H. Central nervous system effects of acetate - contribution to the central effects of ethanol. *Journal of Pharmacology and Experimental Therapeutics*, 1991; 259(1):p403-408.

Carmichael F, Saldivia V, Varghese G, Israel Y, Orrego H. Ethanol-induced increase in portal blood flow: Role of acetate and a1- and a2-adenosine receptors. *American Journal of Physiology*, 1988; 255(4):p417-423.

Carpenter J. Effects of alcohol on some psychological processes. A critical review with special reference to automobile driving skill. *Quarterly Journal of Studies on Alcohol*, 1962; 23:p274-314.

Carter A, Muller R. Hydration knowledge, behaviours and status of staff at the residential camp of a fly-in/fly-out minerals extraction and processing operation in tropical north-eastern australia. *Industrial Health*, 2007; 45(4):p579-589.

Carter A, Muller R, Roberts S. The hydration status and needs of workers at a north-west queensland fertilizer plant. *Journal of Health, Safety and Environment*, 2006; 22(1):p73-82.

Chang Y, Labban J, Gapin J, Etnier J. The effects of acute exercise on cognitive performance: A meta-analysis. *Brain Research*, 2012; 1453:p87-101.

Charlebois R, Corbett M, Wigmore J. Comparison of ethanol concentrations in blood, serum, and blood cells for forensic application. *Journal of Analytical Toxicology*, 1996; 20(3):p171-178.

Cherpitel C. Alcohol, injury, and risk-taking behavior: Data from a national sample. *Alcoholism: Clinical and Experimental Research*, 1993; 17(4):p762-766.

Cherpitel C. Substance use, injury, and risk-taking dispositions in the general population. *Alcoholism: Clinical and Experimental Research*, 1999; 23(1):p121-126.

Chikritzhs T, Jonas H, Heale P, Dietze P, Hanlin K, Stockwell T. *Alcohol-caused deaths and hospitalisations in australia, 1990-1997. National alcohol indicators, bulletin no.1*. National Drug Research Institute, Curtin University of Technology; 1999.

Chikritzhs T, Stockwell T, Heale P, Dietze P, Webb M. *Trends in alcohol-related road injury in australia, 1990-1997. National alcohol indicators, bulletin no.2*. National Drug Research Institute, Curtin University of Technology; 2000.

Cian C, Barraud P, Melin B, Raphel C. Effects of fluid ingestion on cognitive function after heat stress or exercise-induced dehydration. *International Journal of Psychophysiology*, 2001; 42(3):p243-251.

Cian C, Koulmann N, Barraud P, Raphel C, Jimenez C, Melin B. Influence of variations in body hydration on cognitive function: Effect of hyperhydration, heat stress, and exercise-induced dehydration. *Journal of Psychophysiology*, 2000; 14(1):p29-36.

Clapp A, Bishop P, Smith J, Lloyd L, Wright K. A review of fluid replacement for workers in hot jobs. *American Industrial Hygiene Association Journal*, 2002; 63(2):p190-198.

Clapp A, Bishop P, Smith J, Mansfield E. Effects of carbohydrate-electrolyte content of beverages on voluntary hydration in a simulated industrial environment. *American Industrial Hygiene Association Journal*, 2000; 61(5):p692-699.

Clapp A, Bishop P, Walker J. Fluid replacement preferences in heat-exposed workers. *American Industrial Hygiene Association Journal*, 1999; 60(6):p747-751.

Clayton B, Harris J. Our friend jack: Alcohol, friendship and masculinity in university football. *Annals of Leisure Research*, 2008; 11(3-4):p311-330.

Cole-Harding S, Michels V. Does expectancy affect alcohol absorption? *Addictive Behaviors*, 2007; 32(1):p194-198.

Coles K, Tomporowski P. Effects of acute exercise on executive processing, short-term and long-term memory. *Journal of Sports Sciences*, 2008; 26(3):p333-344.

Collardeau M, Brisswalter J, Audiffren M. Effects of a prolonged run on simple reaction time of well trained runners. *Perceptual and Motor Skills*, 2001; 93(3):p679-689.

Collie A, Maruff P. Computerised neuropsychological testing. *British Journal of Sports Medicine*, 2003; 37(1):p2-3.

Collie A, Maruff P, Darby D, McStephen M. The effects of practice on the cognitive test performance of neurologically normal individuals assessed at brief test-retest intervals. *Journal of the International Neuropsychological Society*, 2003; 9(3):p419-428.

Collins R, Gollnisch G, Izzo C. Drinking restraint and alcohol-related outcomes: Exploring the contributions of beverage instructions, beverage content and self-monitoring. *Journal of Studies on Alcohol*, 1996; 57(5):p563-571.

Connor J, Norton R, Ameratunga S, Jackson R. The contribution of alcohol to serious car crash injuries. *Epidemiology*, 2004; 15(3):p337-344.

Cook R, Hersch R, Back A, McPherson T. The prevention of substance abuse among construction workers: A field test of a social-cognitive program. *The Journal of Primary Prevention*, 2004; 25(3):p337-357.

229

Coolican H. *Research methods and statistics in psychology* (4 ed.); 2004. London, UK: Hodder & Stoughton.

Crabb D, Bosron W, Li T. Ethanol metabolism. *Pharmacology and Therapeutics*, 1987; 34(1):p59-73.

Crabbe J, Phillips T, Buck K, Cunningham C, Belknap J. Identifying genes for alcohol and drug sensitivity: Recent progress and future directions. *Trends in Neurosciences*, 1999; 22(4):p173-179.

Creaser J, Ward N, Rakauskas M. *Acute alcohol impairment research in driving simulators*. In Fisher D, Rizzo M, Caird J, Lee J (Eds.), Handbook of driving simulation for engineering, medicine, and psychology; 2011. Boca Raton, FL: CRC Press.

D'Anci K, Vibhakar A, Kanter J, Mahoney C, Taylor H. Voluntary dehydration and cognitive performance in trained college athletes. *Perceptual and Motor Skills*, 2009; 109(1):p251-269.

Daanen H, van de Vliert E, Huang X. Driving performance in cold, warm, and thermoneutral environments. *Applied Ergonomics*, 2003; 34(6):p597-602.

Davidson D, Camara P, Swift R. Behavioral effects and pharmacokinetics of low-dose intravenous alcohol in humans. *Alcoholism: Clinical and Experimental Research*, 1997; 21(7):p1294-1299.

Davies B, Bowen C. Total body water and peak alcohol concentration: A comparative study of young, middle-age, and older females. *Alcoholism: Clinical and Experimental Research*, 1999; 23(6):p969-975.

de-Wit H, Crean J, Richards J. Effects of d-amphetamine and ethanol on a measure of behavioral inhibition in humans. *Behavioral Neuroscience*, 2000; 114(4):p830-837.

Deitrich R, Dunwiddie T, Harris R, Erwin V. Mechanism of action of ethanol: Initial central nervous system actions. *Pharmacological Reviews*, 1989; 41(4):p489-537.

Del Boca F, Darkes J. The validity of self-reports of alcohol consumption: State of the science and challenges for research. *Addiction*, 2003; 98(2 Suppl):p1-12.

Desbrow B, Murray D, Leveritt M. Beer as a sports drink? Manipulating beer's ingredients to replace lost fluid. *International Journal of Sport Nutrition and Exercise Metabolism*, 2013; In Press:p.

Dexter F, Chestnut D. Analysis of statistical tests to compare visual analog scale measurements among groups. *Anesthesiology*, 1995; 82(4):p896-902.

Diabetes Australia. *Diabetes management in general practice: Guidelines for type 2 diabetes*. Pinnacle Print Management, Gorokan, NSW; 2009.

Dill D, Costill D. Calculation of percentage changes in volumes of blood, plasma, and red cells in dehydration. *Journal of Applied Physiology*, 1974; 37(2):p247-248.

Doniger G, Simon E, Zivotofsky A. Comprehensive computerized assessment of cognitive sequelae of a complete 12-16 hour fast. *Behavioral Neuroscience*, 2006; 120(4):p804-816.

Dougherty D, Marsh-Richard D, Hatzis E, Nouvion S, Mathias C. A test of alcohol dose effects on multiple behavioral measures of impulsivity. *Drug and Alcohol Dependence*, 2008; 96(1-2):p111-120.

Downey L, King R, Papafotiou K, Swann P, Ogden E, Boorman M, Stough C. The effects of cannabis and alcohol on simulated driving: Influences of dose and experience. *Accident Analysis & Prevention*, 2013; 50(0):p879-886.

Duff C, Scealy M, Rowland B. *The culture and context of alcohol use in community sporting clubs in australia: Research into 'attitudes' and 'behaviour'*. Centre for Youth Drug Studies, Australian Drug Foundation; 2004.

Dunn M, Wang M. Effects of physical activity on substance use among college students. *American Journal of Health Studies*, 2003; 18(2-3):p126-132.

Durlach P. The effects of a low dose of caffeine on cognitive performance. *Psychopharmacology*, 1998; 140(1):p116-119.

Dwolatzky T, Whitehead V, Doniger G, Simon E, Schweiger A, Jaffe D, Chertkow H. Validity of a novel computerized cognitive battery for mild cognitive impairment. *BMC Geriatrics*, 2003; 3(1):p4-16.

Eckardt M, File S, Gessa G, Grant K, Guerri C, Hoffman P, Kalant H, Koob G, Li T, Tabakoff B. Effects of moderate alcohol consumption on the central nervous system. *Alcoholism: Clinical and Experimental Research*, 1998; 22(5):p998-1040.

Eckardt M, Harford T, Kaelber C, Parker E, Rosenthal L, Ryback R, Salmoiraghi G, Vanderveen E, Warren K. Health hazards associated with alcohol consumption. *Journal of the American Medical Association*, 1981; 246(6):p648-666.

Edwards A, Mann M, Marfell-Jones M, Rankin D, Noakes T, Shillington D. Influence of moderate dehydration on soccer performance: Physiological responses to 45 min of outdoor match-play and the immediate subsequent performance of sport-specific and mental concentration tests. *British Journal of Sports Medicine*, 2007; 41(6):p385-391.

Egerhazi A, Berecz R, Bartok E, Degrell I. Automated neuropsychological test battery (cantab) in mild cognitive impairment and in alzheimer's disease. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, 2007; 31(3):p746-751.

Eggleton M. The diuretic action of alcohol in man. *The Journal of Physiology*, 1942; 101(2):p172-191.

Eisenhofer G, Johnson R. Effects of ethanol ingestion on thirst and fluid consumption in humans. *American Journal of Physiology*, 1983; 244(4):p568-572.

Ekman G, Frankenhaeuser M, Goldberg L, Bjerver K, Järpe G, Myrsten A. Effects of alcohol intake on subjective and objective variables over a five-hour period. *Psychopharmacology*, 1963; 4(1):p28-38.

Elliott R. Executive functions and their disorders. *British Medical Bulletin*, 2003; 65(1):p49-59.

Ely B, Sollanek K, Cheuvront S, Lieberman H, Kenefick R. Hypohydration and acute thermal stress affect mood state but not cognition or dynamic postural balance. *European Journal of Applied Physiology*, 2013; 113(4):p1027-1034.

Emerson V, Holleyhead R, Isaacs M, Fuller N, Hunt D. The measurement of breath alcohol. The laboratory evaluation of substantive breath test equipment and the report of an operational police trial. *Journal of the Forensic Science Society*, 1980; 20(1):p3-70.

Epstein Y, Keren G, Moisseiev J, Gasko O, Yachin S. Psychomotor deterioration during exposure to heat. *Aviation, Space and Environmental Medicine*, 1980; 51(6):p607-610.

Erstad B. Osmolality and osmolarity: Narrowing the terminology gap. *Pharmacotherapy*, 2003; 23(9):p1085-1086.

Etnier J, Salazar W, Landers D, Petruzzello S, Han M, Nowell P. The influence of physical fitness and exercise upon cognitive functioning: A meta-analysis. *Journal of Sport and Exercise Psychology*, 1997; 19(3):p249-277.

European Food Safety Authority. Scientific opinion on dietary reference values for water. Efsa panel on dietetic products, nutrition and allergies. *European Food Safety Authority Journal*, 2010; 8(3):p1459-1460.

Faingold C, N'Gouemo P, Riaz A. Ethanol and neurotransmitter interactions: From molecular to integrative effects. *Progress in Neurobiology*, 1998; 55(5):p509-535.

Farber P, Khavari K, Douglass F. A factor analytic study of reasons for drinking: Empirical validation of positive and negative reinforcement dimensions. *Journal of Consulting & Clinical Psychology*, 1980; 48(6):p780-781.

Fillmore M. Cognitive preoccupation with alcohol and binge drinking in college students: Alcohol-induced priming of the motivation to drink. *Psychology of Addictive Behaviors* 2001; 15(4):p325-332.

Fillmore M. Acute alcohol-induced impairment of cognitive functions: Past and present findings. *International Journal on Disability and Human Development*, 2007; 6(2):p115-125.

Fillmore M, Blackburn J. Compensating for alcohol-induced impairment: Alcohol expectancies and behavioral disinhibition. *Journal of Studies on Alcohol*, 2002; 63(2):p237-246.

Fillmore M, Blackburn J, Harrison E. Acute disinhibiting effects of alcohol as a factor in risky driving behavior. *Drug and Alcohol Dependence*, 2008; 95(1-2):p97-106.

Fillmore M, Carscadden J, Vogel-Sprott M. Alcohol, cognitive impairment and expectancies. *Journal of Studies on Alcohol*, 1998; 59(2):p174-179.

Fillmore M, Dixon M, Schweizer T. Differential effects of alcohol on responses to negatively and positively primed stimuli. *Journal of Studies on Alcohol*, 2000; 61(6):p872-880.

Fillmore M, Vogel-Sprott M. Expectancies about alcohol-induced motor impairment predict individual differences in responses to alcohol and placebo. *Journal of Studies on Alcohol*, 1995; 56(1):p90-98.

Fillmore M, Vogel-Sprott M. Behavioral impairment under alcohol: Cognitive and pharmacokinetic factors. *Alcoholism: Clinical and experimental Research*, 1998; 22(7):p1476-1482.

Fillmore M, Vogel-Sprott M. Response inhibition under alcohol: Effects of cognitive and motivational conflict. *Journal of Studies on Alcohol*, 2000; 61(2):p239-246.

Fillmore M, Weafer J. Alcohol impairment of behavior in men and women. *Addiction*, 2004; 99(10):p1237-1246.

Finnigan F, Hammersley R, Millar K. The effects of expectancy and alcohol on cognitive-motor performance. *Addiction*, 1995; 90(5):p661-672.

Fowler K, Saling M, Conway E, Semple J, Louis W. Computerized neuropsychological tests in the early detection of dementia: Prospective findings. *Journal of the International Neuropsychological Society*, 1997; 3(2):p139-146.

Franke A, Teyssen S, Harder H, Singer M. Effect of ethanol and some alcoholic beverages on gastric emptying in humans. *Scandinavian Journal of Gastroenterology*, 2004; 39(7):p638-644.

Fray P, Robbins T. Cantab battery: Proposed utility in neurotoxicology. *Neurotoxicology and Teratology*, 1996; 18(4):p499-504.

Frezza M, di-Padova C, Pozzato G, Terpin M, Baraona E, Lieber C. High blood alcohol levels in women. The role of decreased gastric alcohol dehydrogenase activity and first-pass metabolism. *The New England Journal of Medicine*, 1990; 322(2):p95-99.

Friedman T, Robinson S, Yelland G. Impaired perceptual judgment at low blood alcohol concentrations. *Alcohol*, 2010; 45(7):p711-718.

Frone M. Work stress and alcohol use. *Alcohol Research & Health*, 1999; 23(4):p284-291.

Galotti K. *Cognitive psychology: In and out of the laboratory* (5 ed.); 2013. SAGE Publications.

Ganio M, Armstrong L, Casa D, McDermott B, Lee E, Yamamoto L, Marzano S, Lopez R, Jimenez L, Le Bellego L, Chevillotte E, Lieberman H. Mild dehydration impairs cognitive performance and mood of men. *British Journal of Nutrition*, 2011; 106(10):p1535-1543.

George S, Rogers R, Duka T. The acute effect of alcohol on decision making in social drinkers. *Psychopharmacology*, 2005; 182(1):p160-169.

Goist Jr K, Sutker P. Acute alcohol intoxication and body composition in women and men. *Pharmacology Biochemistry and Behavior*, 1985; 22(5):p811-814.

Gopinathan P, Pichan G, Sharma V. Role of dehydration in heat stress-induced variations in mental performance. *Archives of Environmental Health*, 1988; 43(1):p15-17.

Grandjean A, Campbell S. *Hydration: Fluids for life. A monograph by the north american branch of the international life science institute*. ILSI North America, Washington DC; 2004.

233

Grandjean A, Grandjean N. Dehydration and cognitive performance. *Journal of the American College of Nutrition*, 2007; 26(5 Suppl):p549-554.

Green M, Elliman N, Rogers P. Lack of effect of short-term fasting on cognitive function. *Journal of Psychiatric Research*, 1995; 29(3):p245-253.

Grego F, Vallier J, Collardeau M, Rousseu C, Cremieux J, Brisswalter J. Influence of exercise duration and hydration status on cognitive function during prolonged cycling exercise. *International Journal of Sports Medicine*, 2005; 26(1):p27-33.

Guillot C, Fanning J, Bullock J, McCloskey M, Berman M. Effects of alcohol on tests of executive functioning in men and women: A dose response examination. *Experimental and Clinical Psychopharmacology*, 2010; 18(5):p409-417.

Hack M, Choi S, Vijayapalan P, Davies R, Stradling J. Comparison of the effects of sleep deprivation, alcohol and obstructive sleep apnoea (osa) on simulated steering performance. *Respiratory Medicine*, 2001; 95(7):p594-601.

Haggard H, Greenberg L, Cohen L. The influence of the congeners of distilled spirits upon the physiological action of alcohol. *Quarterly Journal of Studies on Alcohol*, 1943; 4(1):p3-56.

Haggard H, Greenberg L, Rakieten N. Studies on the absorption, distribution and elimination of alcohol vi the principles governing the concentration of alcohol in the blood and the concentration causing respiratory failure. *Journal of Pharmacology and Experimental Therapeutics*, 1940; 69(3):p252-265.

Hammersley R, Finnigan F, Millar K. Alcohol placebos: You can only fool some of the people all of the time. *British Journal of Addiction*, 1992; 87(10):p1477-1480.

Hammersley R, Finnigan F, Millar K. Verbal expectancies and performance after alcohol. *Addictive Behaviors*, 1998; 23(4):p489-496.

Harding P. *Alcohol toxicology for prosecutors: Targeting hardcore impaired drivers*; 2003. Alexandria, VA: American Prosecutors Research Institute.

Harger R, Forney R, Barnes H. Estimation of the level of blood alcohol from analysis of breath. *The Journal of Laboratory and Clinical Medicine*, 1950; 36(2):p306-318.

Harrison E, Fillmore M. Are bad drivers more impaired by alcohol? Sober driving precision predicts impairment from alcohol in a simulated driving task. *Accident Analysis and Prevention*, 2005; 37(5):p882-889.

Harrison E, Fillmore M. Alcohol and distraction interact to impair driving performance. *Drug and Alcohol Dependence*, 2011; 117(1):p31-37.

Harrison E, Marczinski C, Fillmore M. Driver training conditions affect sensitivity to the impairing effects of alcohol on a simulated driving test. *Experimental and Clinical Psychopharmacology*, 2007; 15(6):p588-598.

Harrison M. Effects of thermal stress and exercise on blood volume in humans. *Physiological Reviews*, 1985; 65(1):p149-209.

Hawkins R, Kalant H. The metabolism of ethanol and its metabolic effects. *Pharmacological Reviews*, 1972; 24(1):p67-157.

Heishman S, Arasteh K, Stitzer M. Comparative effects of alcohol and marijuana on mood, memory, and performance. *Pharmacology, Biochemistry, and Behavior*, 1997; 58(1):p93-101.

Helland A, Jenssen G, Lervag L, Westin A, Moen T, Sakshaug K, Lydersen S, Morland J, Slordal L. Comparison of driving simulator performance with real driving after alcohol intake: A randomised, single blind, placebo-controlled, cross-over trial. *Accident Analysis and Prevention*, 2013; 53:p9-16.

Hindmarch I, Kerr J, Sherwood N. The effects of alcohol and other drugs on psychomotor performance and cognitive function. *Alcohol and Alcoholism*, 1991; 26(1):p71-79.

Hlastala M. The alcohol breath test - a review. *Journal of Applied Physiology*, 1998; 84(2):p401-408.

Hlastala M. Paradigm shift for the alcohol breath test. *Journal of Forensic Sciences*, 2010; 55(2):p451-456.

Hobson R, Maughan R. Hydration status and the diuretic action of a small dose of alcohol. *Alcohol and Alcoholism*, 2010; 45(4):p366-373.

Hogervorst E, Riedel W, Jeukendrup A, Jolles J. Cognitive performance after strenuous physical exercise. *Perceptual and Motor Skills*, 1996; 83(2):p479-488.

Holcomb R. Alcohol in relation to traffic accidents. *Journal of the American Medical Association*, 1938; 111(12):p1076-1085.

Holdstock L, de-Wit H. Individual differences in the biphasic effects of ethanol. *Alcoholism: Clinical and Experimental Research*, 1998; 22(9):p1903-1911.

Holford N. Clinical pharmacokinetics of ethanol. *Clinical Pharmacokinetics*, 1987; 13(5):p273-292.

Horne J, Reyner L, Barrett P. Driving impairment due to sleepiness is exacerbated by low alcohol intake. *Occupational and Environmental Medicine*, 2003; 60(9):p689-692.

Howard M, Jackson M, Kennedy G, Swann P, Barnes M, Pierce R. The interactive effects of extended wakefulness and low-dose alcohol on simulated driving and vigilance. *Sleep*, 2007; 30(10):p1334-1340.

Howland J, Rohsenow D, Arnedt J, Bliss C, Hunt S, Calise T, Heeren T, Winter M, Littlefield C, Gottlieb D. The acute effects of caffeinated versus non-caffeinated alcoholic beverage on driving performance and attention/reaction time. *Addiction*, 2010; 106(2):p335-341.

Hu T, Xie X, Li J. Negative or positive? The effect of emotion and mood on risky driving. *Transportation Research Part F: Traffic Psychology and Behaviour*, 2013; 16:p29-40.

Hubbard R, Sandick B, Matthew W, Francesconi R, Sampson J, Durkot M, Maller O, Engell D. Voluntary dehydration and alliesthesia for water. *Journal of Applied Physiology*, 1984; 57(3):p868-873.

Huemer A, Vollrath M. Alcohol-related impairment in the lane change task. *Accident Analysis and Prevention*, 2010; 42(6):p1983-1988.

Hull J, Bond C. Social and behavioral consequences of alcohol-consumption and expectancy: A meta-analysis. *Psychological Bulletin*, 1986; 99(3):p347-360.

Hunt A, Stewart I, Parker T. *Dehydration is a health and safety concern for surface mine workers*. Institute of Health and Biomedical Innovation: Queensland University of Technology, Brisbane, QLD; 2011.

Iudice A, Bonanni E, Gelli A, Frittelli C, Iudice G, Cignoni F, Ghicopulos I, Murri L. Effects of prolonged wakefulness combined with alcohol and hands-free cell phone divided attention tasks on simulated driving. *Human Psychopharmacology*, 2005; 20(2):p125-132.

Jacobsen E. The metabolism of ethyl alcohol. *Pharmacological Reviews*, 1952; 4(2):p107-135.

Janes C, Ames G. Men, blue collar work and drinking: Alcohol use in an industrial subculture. *Culture, Medicine and Psychiatry*, 1989; 13(3):p245-274.

Jellinek E, Jolliffe N. Effects of alcohol on the individual: Review of the literature of 1939. *Quarterly Journal of Studies on Alcohol*, 1940; 1(1):p110-181.

Jellinek E, McFarland R. Analysis of psychological experiments on the effects of alcohol. *Quarterly Journal of Studies on Alcohol*, 1940; 1(2):p272-371.

Jennings J, Wood C, Lawrence B. Effects of graded doses of alcohol on speed-accuracy tradeoff in choice reaction time. *Attention, Perception and Psychophysics*, 1976; 19(1):p85-91.

Jequier E, Constant F. Water as an essential nutrient: The physiological basis of hydration. *European Journal of Clinical Nutrition*, 2010; 64(2):p115-123.

Jiménez-Pavón D, Romeo J, Cervantes-Borunda M, Ortega F, Ruiz J, España-Romero V, Marcos A, Castillo M. Effects of a running bout in the heat on cognitive performance. *Journal of Exercise Science & Fitness*, 2011; 9(1):p58-64.

Jones A. Variability of the blood:Breath alcohol ratio in vivo. *Journal of Studies on Alcohol*, 1978; 39(11):p1931-1939.

Jones A. Interindividual variations in the disposition and metabolism of ethanol in healthy men. *Alcohol*, 1984; 1(5):p385-391.

Jones A. *Road safety web publication no. 15: The relationship between blood alcohol concentration (bac) and breath alcohol concentration (brac): A review of the evidence*. Department for Transport, London, UK; 2010.

Jones A, Andersson L. Variability of the blood/breath alcohol ratio in drinking drivers. *Journal of Forensic Sciences*, 1996; 41(6):p916-921.

Jones A, Andersson L. Comparison of ethanol concentrations in venous blood and end-expired breath during a controlled drinking study. *Forensic Science International*, 2003; 132(1):p18-25.

Jones A, Jönsson K. Between-subject and within-subject variations in the pharmacokinetics of ethanol. *British Journal of Clinical Pharmacology*, 1994; 37(5):p427-431.

Jones A, Jönsson K, Kechagias S. Effect of high-fat, high-protein, and high-carbohydrate meals on the pharmacokinetics of a small dose of ethanol. *British Journal of Clinical Pharmacology*, 1997; 44(6):p521-526.

Kampmann B, Kalkowsky B, Piekarski C. Dehydration and rehydration of coal miners during work at hot places. *Environmental Ergonomics VIII*, 1998; 1:p43-46.

Kanarek R, Swinney D. Effects of food snacks on cognitive performance in male college students. *Appetite*, 1990; 14(1):p15-27.

Kavouras S. Assessing hydration status. *Current Opinion in Clinical Nutrition and Metabolic Care*, 2002; 5(5):p519-524.

Kempton M, Ettinger U, Foster R, Williams S, Calvert G, Hampshire A, Zelaya F, O'Gorman R, McMorris T, Owen A, Smith M. Dehydration affects brain structure and function in healthy adolescents. *Human Brain Mapping*, 2011; 32(1):p71-79.

Kempton M, Ettinger U, Schmechtig A, Winter E, Smith L, McMorris T, Wilkinson I, Williams S, Smith M. Effects of acute dehydration on brain morphology in healthy humans. *Human Brain Mapping*, 2009; 30(1):p291-298.

Kenefick R, Hazzard M, Armstrong L. *Minor heat illnesses*. In Armstrong L (Ed.), Exertional heat illnesses; 2003 (p137-150). Champaign, IL, USA: Human Kinetics Publishers Inc.

Kenefick R, Sawka M. Hydration at the work site. *Journal of the American College of Nutrition*, 2007; 26(5 Suppl):p597-603.

Kimberlin C, Winterstein A. Validity and reliability of measurement instruments used in research. *American Journal of Health System Pharmacy*, 2008; 65(23):p2276-2284.

King A, Houle T, de Wit H, Holdstock L, Schuster A. Biphasic alcohol response differs in heavy versus light drinkers. *Alcoholism: Clinical and Experimental Research*, 2002; 26(6):p827-835.

Klarica A. Performance in motor sports. *British Journal of Sports Medicine*, 2001; 35(5):p290-291.

Lambourne K, Tomporowski P. The effect of exercise-induced arousal on cognitive task performance: A meta-regression analysis. *Brain Research*, 2010; 1341:p12-24.

Lane S, Cherek D, Pietras C, Tcheremissine O. Alcohol effects on human risk taking. *Psychopharmacology*, 2004; 172(1):p68-77.

Lange K, Robbins T, Marsden C, James M, Owen A, Paul G. L-dopa withdrawal in parkinson's disease selectively impairs cognitive performance in tests sensitive to frontal lobe dysfunction. *Psychopharmacology*, 1992; 107(2):p394-404.

237

Lanza-Kaduce L, Bishop D, Winner L. Risk/benefit calculations, moral evaluations, and alcohol use: Exploring the alcohol-crime connection. *Crime and Delinquency*, 1997; 43(2):p222-239.

Leatherbarrow R. Using linear and non-linear regression to fit biochemical data. *Trends in Biochemical Sciences*, 1990; 15(12):p455-458.

Lee H, Cameron D, Lee A. Assessing the driving performance of older adult drivers: On-road versus simulated driving. *Accident Analysis and Prevention*, 2003; 35(5):p797-803.

Lee H, Roh S, Kim D. Alcohol-induced blackout. *International Journal of Environmental Research and Public Health*, 2009; 6(11):p2783-2792.

Leibowitz H, Abernethy C, Buskirk E, Bar-Or O, Hennessy R. The effect of heat stress on reaction time to centrally and peripherally presented stimuli. *Human Factors*, 1972; 14(2):p155-160.

Lelevich S, Lelevich V, Doroshenko E. Neurotransmitter changes in rat brain following acute alcohol intoxication. *Neurochemical Journal*, 2010; 4(2):p137-141.

Lenne M, Dietze P, Rumbold G, Redman J, Triggs T. The effects of the opioid pharmacotherapies methadone, laam and buprenorphine, alone and in combination with alcohol, on simulated driving. *Drug and Alcohol Dependence*, 2003; 72(3):p271-278.

Lenné M, Dietze P, Triggs T, Walmsley S, Murphy B, Redman J. The effects of cannabis and alcohol on simulated arterial driving: Influences of driving experience and task demand. *Accident Analysis and Prevention*, 2010; 42(3):p859-866.

Lennernas M, Hambraeus L, Akerstedt T. Shift related dietary intake in day and shift workers. *Appetite*, 1995; 25(3):p253-265.

Lex B, Greenwald N, Lukas S, Slater J, Mendelson J. Blood ethanol levels, self-rated ethanol effects and cognitive-perceptual tasks. *Pharmacology, Biochemistry, and Behavior*, 1988; 29(3):p509-515.

Li T, Yin S, Crabb D, O'Connor S, Ramchandani V. Genetic and environmental influences on alcohol metabolism in humans. *Alcoholism: Clinical and Experimental Research*, 2001; 25(1):p136-144.

Liang T, Spence J, Liu L, Strother W, Chang H, Ellison J, Lumeng L, Li T, Foroud T, Carr L. Alpha-synuclein maps to a quantitative trait locus for alcohol preference and is differentially expressed in alcohol-preferring and -nonpreferring rats. *Proceedings of the National Academy of Sciences of the United States of America*, 2003; 100(8):p4690-4695.

Lieber C. Metabolism of alcohol. *Clinics in Liver Disease*, 2005; 9(1):p1-35.

Lieberman H. Hydration and cognition: A critical review and recommendations for future research. *Journal of the American College of Nutrition*, 2007; 26(5 Suppl):p555-561.

Lieberman H. Hydration and human cognition. *Nutrition Today*, 2010; 45(6 Suppl):p33-36.

Lieberman H. Methods for assessing the effects of dehydration on cognitive function. *Nutrition Reviews*, 2012; 70(2 Suppl):p143-146.

Liguori A, D'Agostino R, Dworkin S, Edwards D, Robinson J. Alcohol effects on mood, equilibrium, and simulated driving. *Alcoholism: Clinical and Experimental Research*, 1999; 23(5):p815-821.

Liguori A, Gatto C, Jarrett D. Separate and combined effects of marijuana and alcohol on mood, equilibrium and simulated driving. *Psychopharmacology*, 2002; 163(3-4):p399-405.

Liguori A, Robinson J. Caffeine antagonism of alcohol-induced driving impairment. *Drug and Alcohol Dependence*, 2001; 63(2):p123-129.

Lin Y, Weidler D, Garg D, Wagner J. Effects of solid food on blood levels of alcohol in man. *Research Communications in Chemical Pathology and Pharmacology*, 1976; 13(4):p713-722.

Lindberg L, Brauer S, Wollmer P, Goldberg L, Jones A, Olsson S. Breath alcohol concentration determined with a new analyzer using free exhalation predicts almost precisely the arterial blood alcohol concentration. *Forensic Science International*, 2007; 168(2-3):p200-207.

Linkola J, Ylikahri R, Fyhquist F, Wallenius M. Plasma vasopressin in ethanol intoxication and hangover. *Acta Physiologica Scandinavica*, 1978; 104(2):p180-187.

Liu Y, Fu S. Changes in driving behavior and cognitive performance with different breath alcohol concentration levels. *Traffic Injury Prevention*, 2007; 8(2):p153-161.

Liu Y, Ho C. Effects of different blood alcohol concentrations and post-alcohol impairment on driving behavior and task performance. *Traffic Injury Prevention*, 2010; 11(4):p334-341.

Lloyd H, Rogers P. Mood and cognitive performance improved by a small amount of alcohol given with a lunchtime meal. *Behavioural Pharmacology*, 1997; 8(2-3):p188-195.

Loeber S, Duka T. Acute alcohol impairs conditioning of a behavioural reward-seeking response and inhibitory control processes: Implications for addictive disorders. *Addiction*, 2009; 104(12):p2013-2022.

Lolli G, Rubin M. The effect of concentration of alcohol on the rate of absorption and the shape of the blood alcohol curve. *Quarterly Journal of Studies on Alcohol*, 1943; 4(1):p57-63.

London L. Alcohol consumption amongst south african farm workers: A challenge for post-apartheid health sector transformation. *Drug and Alcohol Dependence*, 2000; 59(2):p199-206.

Louis W, Mander A, Dawson M, O'Callaghan C, Conway E. Use of computerized neuropsychological tests (cantab) to assess cognitive effects of antihypertensive drugs in the elderly. *Journal of Hypertension*, 1999; 17(12):p1813-1819.

Lowe C, Rabbitt P. Test/re-test reliability of the cantab and ispocd neuropsychological batteries: Theoretical and practical issues. Cambridge neuropsychological test automated battery. International study of post-operative cognitive dysfunction. *Neuropsychologia*, 1998; 36(9):p915-923.

Lucey M, Hill E, Young J, Demo-Dananberg L, Beresford T. The influences of age and gender on blood ethanol concentrations in healthy humans. *Journal of Studies on Alcohol*, 1999; 60(1):p103-110.

Ludbrook J. Comparing methods of measurements. *Clinincal and Experimental Pharmacology and Physiology*, 1997; 24(2):p193-203.

Lyvers M, Maltzman I. Selective effects of alcohol on wisconsin card sorting test performance. *British Journal of Addiction*, 1991; 86(4):p399-407.

MacArthur R, Sekuler R. Alcohol and motion perception. *Perception and Psychophysics*, 1982; 31(5):p502-505.

Mackie R, O'Hanlon J. *A study of the combined effects of extended driving and heat stress on driver arousal and performance*. In Mackie R (Ed.), Vigilance; 1977 (Vol. 3, p537-558): Springer US.

MacLeod C. *The concept of inhibition in cognition*. In Gorfein D, MacLeod C (Eds.), Inhibition in cognition; 2007 (p3-23). Washington, DC: American Psychological Association.

MacLeod H, Sunderland C. Previous-day hypohydration impairs skill performance in elite female field hockey players. *Scandinavian Journal of Medicine & Science in Sports*, 2012; 22(3):p430-438.

Makela P, Wakeley J, Gijsman H, Robson P, Bhagwagar Z, Rogers R. Low doses of delta-9 tetrahydrocannabinol (thc) have divergent effects on short-term spatial memory in young, healthy adults. *Neuropsychopharmacology*, 2005; 31(2):p462-470.

Mantyla T, Karlsson M, Marklund M. Executive control functions in simulated driving. *Applied Neuropsychology*, 2009; 16(1):p11-18.

Marcotte T, Roberts E, Rosenthal T, Heaton R, Bentley H, Grant I. Test-retest reliability of standard deviation of lane position as assessed on a pc-based driving simulator. *Proceedings of the Second International Driving Symposium on Human Factors in Driver Assessment, Training and Vehicle Design,* 2003; Park City, Utah, p199-200.

Marczinski C, Abroms B, Van Selst M, Fillmore M. Alcohol-induced impairment of behavioral control: Differential effects on engaging vs disengaging responses. *Psychopharmacology*, 2005; 182(3):p452-459.

Marczinski C, Fillmore M. Pre-response cues reduce the impairing effects of alcohol on the execution and suppression of responses. *Experimental and Clinical Psychopharmacology*, 2003; 11(1):p110-117.

Marczinski C, Fillmore M. Acute alcohol tolerance on subjective intoxication and simulated driving performance in binge drinkers. *Psychology of Addictive Behaviors*, 2009; 23(2):p238-247.

Marczinski C, Harrison E, Fillmore M. Effects of alcohol on simulated driving and perceived driving impairment in binge drinkers. *Alcoholism: Clinical and Experimental Research*, 2008; 32(7):p1329-1337.

Marczinski C, Stamates A. Artificial sweeteners versus regular mixers increase breath alcohol concentrations in male and female social drinkers. *Alcoholism: Clinical and Experimental Research*, 2013; 37(4):p696-702.

Marieb E, Hoehn K. *Human anatomy & physiology*; 2007. Pearson Benjamin Cummings.

Markovsky M. Avoiding dehydration in the workplace. *Water Conditioning & Purification*, 2010; 52(9):p46-50.

Marlatt G, Rohsenow D. *Cognitive processes in alcohol use: Expectancy and the balanced placebo design*. In Mello N (Ed.), Advances in substance abuse: Behavioral and biological research; 1980 (Vol. 1, p159-199). Greenwich, CT: JAI Press.

Marsh-Richard D, Hatzis E, Mathias C, Venditti N, Dougherty D. Adaptive visual analog scales (avas): A modifiable software program for the creation, administration, and scoring of visual analog scales. *Behavior Research Methods*, 2009; 41(1):p99-106.

Marshall A, Kingstone D, Boss M, Morgan M. Ethanol elimination in males and females: Relationship to menstrual cycle and body composition. *Hepatology*, 1983; 3(5):p701-706.

Martens M, Dams-O'Connor K, Beck N. A systematic review of college student-athlete drinking: Prevalence rates, sport-related factors, and interventions. *Journal of Substance Abuse Treatment*, 2006; 31(3):p305-316.

Martin C, Earleywine M, Musty R, Perrine M, Swift R. Development and validation of the biphasic alcohol effects scale. *Alcoholism: Clinical and Experimental Research*, 1993; 17(1):p140-146.

Martin E, Moll W, Schmid P, Dettli L. The pharmacokinetics of alcohol in human breath, venous and arterial blood after oral ingestion. *European Journal of Clinical Pharmacology*, 1984; 26(5):p619-626.

Mason M, Dubowski K. Breath-alcohol analysis: Uses, methods, and some forensic problems - review and opinion. *Journal of Forensic Sciences*, 1976; 21(1):p9-41.

Matthews G, Saxby D, Funke G, Emo A, Desmond P. *Driving in states of fatigue or stress*. In Fisher D, Rizzo M, Caird J, Lee J (Eds.), Handbook of driving simulation for engineering, medicine, and psychology; 2011. Boca Raton, FL: CRC Press.

Maughan R. Impact of mild dehydration on wellness and on exercise performance. *European Journal of Clinical Nutrition*, 2003; 57(2 Suppl):p19-23.

Maughan R, Fallah J, Coyle E. The effects of fasting on metabolism and performance. *British Journal of Sports Medicine*, 2010; 44(7):p490-494.

Maughan R, Shirreffs S, Leiper J. Errors in the estimation of hydration status from changes in body mass. *Journal of Sports Sciences*, 2007; 25(7):p797-804.

Maughan R, Shirreffs S, Watson P. Exercise, heat, hydration and the brain. *Journal of the American College of Nutrition*, 2007; 26(5 Suppl):p604-612.

Maughan R, Watson P, Evans G, Broad N, Shirreffs S. Water balance and salt losses in competitive football. *International Journal of Sport Nutrition and Exercise Metabolism*, 2007; 17(6):p583-594.

Maxwell C. Sensitivity and accuracy of the visual analogue scale: A psycho-physical classroom experiment. *British Journal of Clinical Pharmacology*, 1978; 6(1):p15-24.

Maylor E, Rabbitt P. Alcohol, reaction-time and memory: A meta-analysis. *British Journal of Psychology*, 1993; 84(3):p301-317.

Maylor E, Rabbitt P, Sahgal A, Wright C. Effects of alcohol on speed and accuracy in choice reaction time and visual search. *Acta Psychologica*, 1987; 65(2):p147-163.

McKinley M, Johnson A. The physiological regulation of thirst and fluid intake. *News in Physiological Sciences*, 2004; 19(1):p1-6.

McMillen D, Smith S, Wellsparker E. The effects of alcohol, expectancy, and sensation seeking on driving risk-taking. *Addictive Behaviors*, 1989; 14(4):p477-483.

McMorris T, Swain J, Smith M, Corbett J, Delves S, Sale C, Harris R, Potter J. Heat stress, plasma concentrations of adrenaline, noradrenaline, 5-hydroxytryptamine and cortisol, mood state and cognitive performance. *International Journal of Psychophysiology*, 2006; 61(2):p204-215.

Meda S, Calhoun V, Astur R, Turner B, Ruopp K, Pearlson G. Alcohol dose effects on brain circuits during simulated driving: An fmri study. *Human Brain Mapping*, 2009; 30(4):p1257-1270.

Meister K, Whelan E, Kava R. The health effects of moderate alcohol intake in humans: An epidemiologic review. *Critical Reviews in Clinical Laboratory Sciences*, 2000; 37(3):p261-296.

Mets M, Kuipers E, de-Senerpont Domis L, Leenders M, Olivier B, Verster J. Effects of alcohol on highway driving in the stisim driving simulator. *Human Psychopharmacology*, 2011; 26(6):p434-439.

Miles W. Some psycho-physiological processes as affected by alcohol. *Proceedings of the National Academy of Sciences of the United States of America*, 1916; 2:p703-709.

Miles W. The comparative concentrations of alcohol in human blood and urine at intervals after ingestion. *Journal of Pharmacology and Experimental Therapeutics*, 1922; 20(4):p265-319.

Miles W. Action of dilute alcohol on human subjects. *Proceedings of the National Academy of Sciences of the United States of America*, 1924; 10:p333-336.

Millar K, Hammersley R, Finnigan F. Reduction of alcohol-induced performance impairment by prior ingestion of food. *British Journal of Psychology*, 1992; 83(2):p261-278.

Miller V, Bates G. Hydration of outdoor workers in north-west australia. *Journal of Health, Safety and Environment*, 2007; 23(1):p79-87.

Miller V, Bates G. Hydration, hydration, hydration. *Annals of Occupational Hygiene*, 2010; 54(2):p134-136.

Mitchell M. Alcohol-induced impairment of central nervous system function: Behavioral skills involved in driving. *Journal of Studies on Alcohol*, 1985; 10:p109-116.

Moller H. *Psychiatric disorders and driving performance*. In Fisher D, Rizzo M, Caird J, Lee J (Eds.), Handbook of driving simulation for engineering, medicine, and psychology; 2011. Boca Raton, FL: CRC Press.

Morioka I, Miyai N, Miyashita K. Hot environment and health problems of outdoor workers at a construction site. *Industrial Health*, 2006; 44(3):p474-480.

Morley J, Beauchamp G, Suyama J, Guyette F, Reis S, Callaway C, Hostler D. Cognitive function following treadmill exercise in thermal protective clothing. *European Journal of Applied Physiology*, 2012; 112(5):p1733-1740.

Moselhy H, Georgiou G, Kahn A. Frontal lobe changes in alcoholism: A review of the literature. *Alcohol and Alcoholism*, 2001; 36(5):p357-368.

Moskowitz H, Burns M. Effects of alcohol on driving performance. *Alcohol Health and Research World*, 1990; 14(1):p12-15.

Moskowitz H, Fiorentino D. *A review of the literature on the effects of low doses of alcohol on driving-related skills*. National Highway Traffic Safety Administration, Washington, DC; 2000. DOT HS 809 028.

Moskowitz H, Robinson C. *Effects of low doses of alcohol on driving-related skills: A review of the evidence*. National Highway Traffic Safety Administration, Washington, DC; 1988. DOT HS 807 280.

Mukherjee S, Das S, Vaidyanathan K, Vasudevan D. Consequences of alcohol consumption on neurotransmitters: An overview. *Current Neurovascular Research*, 2008; 5(4):p266-272.

Mullen N, Charlton J, Devlin A, Bedard M. *Simulator validity: Behaviours observed on the simulator and on the road*. In Fisher D, Rizzo M, Caird J, Lee J (Eds.), Handbook of driving simulation for engineering, medicine, and psychology; 2011. Boca Raton, FL: CRC Press.

Mulvihill L, Skilling T, Vogel-Sprott M. Alcohol and the ability to inhibit behavior in men and women. *Journal of Studies on Alcohol*, 1997; 58(6):p600-605.

Mumenthaler M, Taylor J, O'Hara R, Yesavage J. Gender differences in moderate drinking effects. *Alcohol Research and Health*, 1999; 23(1):p55-64.

Murray B. Hydration and physical performance. *Journal of the American College of Nutrition*, 2007; 26(5 Suppl):p542-548.

Murray M. The diuretic action of alcohol and its relation to pituitrin. *The Journal of Physiology*, 1932; 76(3):p379-386.

Musselman J, Rutledge P. The incongruous alcohol-activity association: Physical activity and alcohol consumption in college students. *Psychology of Sport and Exercise*, 2010; 11(6):p609-618.

National Health and Medical Research Council. *Nutrient reference values for australia and new zealand: Including recommended dietary intakes*. Department of Health and Ageing: Australian Government, 2005.

National Health and Medical Research Council. *Australian guidelines, to reduce health risks from drinking alcohol*. Commonwealth of Australia, 2009.

Neave N, Scholey A, Emmett J, Moss M, Kennedy D, Wesnes K. Water ingestion improves subjective alertness, but has no effect on cognitive performance in dehydrated healthy young volunteers. *Appetite*, 2001; 37(3):p255-256.

Neisser U. *Cognitive psychology*; 1967. Appleton Century Crofts.

New South Wales Office of Drug Policy. *Nsw alcohol summit: Preliminary background paper*. The Cabinet Office, 2003.

Newell A, Carmichael A, Gregor P, Alm N. *Information technology for cognitive support*. In Jacko J, Sears A (Eds.), The human-computer interaction handbook; 2003 (p464-481). New Jersey: L. Erlbaum Associates Inc.

Newman H, Abramson M. Absorption of various alcoholic beverages. *Science*, 1942; 96(2480):p43-44.

Nicholson M, Wang M, Airhihenbuwa C, Mahoney B, Maney D. Predicting alcohol impairment: Perceived intoxication versus bac. *Alcoholism: Clinical and Experimental Research*, 1992; 16(4):p747-750.

O'Brien C, Lyons F. Alcohol and the athlete. *Sports Medicine*, 2000; 29(5):p295-300.

O'Connor S, Morzorati S, Christian J, Li T. Clamping breath alcohol concentration reduces experimental variance: Application to the study of acute tolerance to alcohol and alcohol elimination rate. *Alcoholism: Clinical and Experimental Research*, 1998; 22(1):p202-210.

O'Neill B, Williams A, Dubowski K. Variability in blood alcohol concentrations. Implications for estimating individual results. *Journal of Studies on Alcohol*, 1983; 44(2):p222-230.

Office of the Queensland Parliamentary Counsel. *Transport operations (road use management) act 1995*. Queensland Government, Queensland, Australia; 2011.

Ogden E, Moskowitz H. Effects of alcohol and other drugs on driver performance. *Traffic Injury Prevention*, 2004; 5(3):p185-198.

Oppliger R, Bartok C. Hydration testing of athletes. *Sports Medicine*, 2002; 32(15):p959-971.

Orrego H, Carmichael F, Israel Y. New insights on the mechanism of the alcohol-induced increase in portal blood flow. *Canadian Journal of Physiology and Pharmacology*, 1988; 66(1):p1-9.

Orrego H, Carmichael F, Saldivia V, Giles H, Sandrin S, Israel Y. Ethanol-induced increase in portal blood flow: Role of adenosine. *American Journal of Physiology*, 1988; 254(4):p495-501.

Oscar-Berman M, Marinkovic K. Alcoholism and the brain: An overview. *Alcohol Research and Health*, 2003; 27(2):p125-133.

Oscar-Berman M, Marinkovic K. Alcohol: Effects on neurobehavioral functions and the brain. *Neuropsychology Review*, 2007; 17(3):p239-257.

Parker R, Ashby L, Bates G. *Dehydration in loggers - a pilot study*. Rotorua, New Zealand; 2001.

Parker R, Ashby L, Bates G. *Dehydration of loggers: Effects of season and time of day*. Rotorua, New Zealand; 2002.

Patel A, Mihalik J, Notebaert A, Guskiewicz K, Prentice W. Neuropsychological performance, postural stability, and symptoms after dehydration. *Journal of Athletic Training*, 2007; 42(1):p66-75.

Paton A. Alcohol in the body. *British Medical Journal*, 2005; 330:p85-87.

Pawan G. Metabolism of alcohol (ethanol) in man. *Proceedings of the Nutrition Society*, 1972; 31(2):p83-89.

Peleg K, Gopher A, Jaffe D, Siman-Tov M, Almog S. Comparison of blood alcohol levels with breath alcohol levels measured using the drager 7110 mkiii breathalyzer. *Injury Prevention*, 2010; 16(1 Suppl):p147-148.

Peterson J, Rothfleisch J, Zelazo P, Pihl R. Acute alcohol intoxication and cognitive functioning. *Journal of Studies on Alcohol*, 1990; 51(2):p114-122.

Petri N, Dropulic N, Kardum G. Effects of voluntary fluid intake deprivation on mental and psychomotor performance. *Croatian Medical Journal*, 2006; 47(6):p855-861.

Philip B. Parametric statistics for evaluation of the visual analog scale. *Anesthesia and Analgesia*, 1990; 71(6):p710.

Pihl R, Paylan S, Gentes-Hawn A, Hoaken P. Alcohol affects executive cognitive functioning differentially on the ascending versus descending limb of the blood alcohol concentration curve. *Alcoholism: Clinical and Experimental Research*, 2003; 27(5):p773-779.

Pikaar N, Wedel M, Hermus R. Influence of several factors on blood alcohol concentrations after drinking alcohol. *Alcohol and Alcoholism*, 1988; 23(4):p289-297.

Pohorecky L. Biphasic action of ethanol. *Biobehavioral Reviews*, 1977; 1(4):p231-240.

Pohorecky L, Brick J. Pharmacology of ethanol. *Pharmacology and Therapeutics*, 1988; 36(2):p335-427.

Popkin B, D'Anci K, Rosenberg I. Water, hydration, and health. *Nutrition Reviews*, 2010; 68(8):p439-458.

Popowski L, Oppliger R, Lambert P, Johnson R, Johnson K, Gisolf C. Blood and urinary measures of hydration status during progressive acute dehydration. *Medicine and Science in Sports and Exercise*, 2001; 33(5):p747-753.

Pross N, Demazieres A, Girard N, Barnouin R, Santoro F, Chevillotte E, Klein A, Le Bellego L. Influence of progressive fluid restriction on mood and physiological markers of dehydration in women. *British Journal of Nutrition*, 2012:p1-9.

Quillian W, Cox D, Kovatchev B, Phillips C. The effects of age and alcohol intoxication on simulated driving performance, awareness and self-restraint. *Age and Ageing*, 1999; 28(1):p59-66.

Rabbitt P, Vyas S. An elementary preliminary taxonomy for some errors in laboratory choice rt tasks. *Acta Psychologica*, 1970; 33:p56-76.

Rakauskas M, Ward N, Boer E, Bernat E, Cadwallader M, Patrick C. Combined effects of alcohol and distraction on driving performance. *Accident Analysis and Prevention*, 2008; 40(5):p1742-1749.

Ramaekers J, Robbe H, O'Hanlon J. Marijuana, alcohol and actual driving performance. *Human Psychopharmacology*, 2000; 15(7):p551-558.

Ramchandani V, Bosron W, Li T. Research advances in ethanol metabolism. *Pathologie Biologie*, 2001; 49(9):p676-682.

Ramchandani V, Kwo P, Li T. Effect of food and food composition on alcohol elimination rates in healthy men and women. *Journal of Clinical Pharmacology*, 2001; 41(12):p1345-1350.

Ramchandani V, O'Connor S. Studying alcohol elimination using the alcohol clamp method. *Alcohol Research and Health*, 2006; 29(4):p286-290.

Retting R, Weinstein H, Solomon M. Analysis of motor-vehicle crashes at stop signs in four u.S. Cities. *Journal of Safety Research*, 2003; 34(5):p485-489.

Rimm D, Sininger R, Faherty J, Whitley M, Perl M. A balanced placebo investigation of the effects of alcohol vs alcohol expectancy on simulated driving behavior. *Addictive Behaviors*, 1982; 7(1):p27-32.

Ritz P, Berrut G. The importance of good hydration for day-to-day health. *Nutrition Reviews*, 2005; 63(6 Suppl):p6-13.

Road Traffic Authority. *Road traffic crashes in new south wales: Statistical statement for the year ended 31 december 2006*. Information Section: NSW Centre for Road Safety, 2007.

Robbe H. Marijuana's impairing effects on driving are moderate when taken alone but severe when combined with alcohol. *Human Psychopharmacology*, 1998; 13(2 Suppl):p70-78.

Robbins T, Jame M, Owen A, Sahakian B, Lawrence A, McInnes L, Rabbitt P. A study of performance on tests from the cantab battery sensitive to frontal lobe dysfunction in a large sample of normal volunteers: Implications for theories of executive functioning and cognitive aging. *Journal of the International Neuropsychological Society*, 1998; 4(5):p474-490.

Robbins T, James M, Owen A, Sahakian B, McInnes L, Rabbitt P. Cambridge neuropsychological test automated battery (cantab): A factor analytic study of a large sample of normal elderly volunteers. *Dementia and Geriatric Cognitive Disorders*, 1994; 5(5):p266-281.

Roberts C, Robinson S. Alcohol concentration and carbonation of drinks: The effect on blood alcohol levels. *Journal of Forensic and Legal Medicine*, 2007; 14(7):p398-405.

Rodrigues L, Magalhães F. Car racing: In the heat of competition. *Revista Brasileira de Medicina do Esporte*, 2004; 10(3):p212-215.

Rohsenow D. Drinking habits and expectancies about alcohol's effects for self versus others. *Journal of Consulting and Clinical Psychology*, 1983; 51(5):p752-756.

Rohsenow D, Marlatt G. The balanced placebo design: Methodological considerations. *Addictive Behaviors*, 1981; 6(2):p107-122.

Roine R, Gentry R, Lim R, Baraona E, Lieber C. Effect of concentration of ingested ethanol on blood-alcohol levels. *Alcoholism: Clinical and Experimental Research*, 1991; 15(4):p734-738.

Roine R, Gentry R, Lim R, Helkkonen E, Salaspuro M, Lieber C. Comparisions of blood-alcohol concentrations after beer and whiskey. *Alcoholism: Clinical and Experimental Research*, 1993; 17(3):p709-711.

Ronen A, Chassidim H, Gershon P, Parmet Y, Rabinovich A, Bar-Hamburger R, Cassuto Y, Shinar D. The effect of alcohol, thc and their combination on perceived effects, willingness to drive and performance of driving and non-driving tasks. *Accident Analysis and Prevention*, 2010; 42(6):p1855-1865.

Ronen A, Gershon P, Drobiner H, Rabinovich A, Bar-Hamburger R, Mechoulam R, Cassuto Y, Shinar D. Effects of thc on driving performance, physiological state and subjective feelings relative to alcohol. *Accident Analysis and Prevention*, 2008; 40(3):p926-934.

Rose S, Furton K. *Variables affecting the accuracy and precision of breath alcohol instruments including the intozilyzer 5000*. In Stein G (Ed.), Georgia dui law, a resource for lawyers and judges; 2004. Georgia: Michie.

Ross C, Weller K. Development of a low-alcohol drink similar in sensory properties to a full-alcohol drink. *Journal of Alcohol and Drug Education*, 2008; 52(3):p37-45.

Rothfusz L. *The heat index 'equation' (or, more than you ever wanted to know about heat index)*. Scientific Services Division (NWS Southern Region Headquarters), Fort Worth, TX, USA; 1990.

Rudin-Brown C, Williamson A, Lenne M. *Can driving simulation be used to predict changes in real-world crash risk?* Monash University: Accident Research Centre, Victoria, Australia; 2009.

Rupp T, Acebo C, Seifer R, Carskadon M. Effects of a moderate evening alcohol dose. Ii: Performance. *Alcoholism: Clinical and Experimental Research*, 2007; 31(8):p1365-1371.

San José B, van de Mheen H, van Oers J, Mackenbach J, Garretsen H. Adverse working conditions and alcohol use in men and women. *Alcoholism: Clinical and Experimental Research*, 2000; 24(8):p1207-1213.

Sawka M. *Water. In panel on dietary reference intakes for electrolytes and water (eds.) "dietary reference intakes for water, potassium, sodium, chloride, and sulfate"*. National Acadamies Press Inc, Washington, DC; 2004.

Sawka M, Burke L, Eichner E, Maughan R, Montain S, Stachenfeld N. American college of sports medicine position stand. Exercise and fluid replacement. *Medicine and Science in Sports and Exercise*, 2007; 39(2):p377-390.

Sawka M, Coyle E. Influence of body water and blood volume on thermoregulation and exercise performance in the heat. *Exercise and Sport Sciences Reviews*, 1999; 27:p167-218.

Schmidt V, Oehmichen M. Alcohol kinetics and constitution types with special reference to its modification by food intake. Experimental studies using parenteral alcohol administration. *Blutalkohol*, 1985; 22(3):p224-232.

Schønheyder F, Petersen O, Terkildsen K, Petersen V. On the variation of the alcoholemic curve. *Acta Medica Scandinavica*, 1942; 109(5-6):p460-470.

Schuckit M, Smith T, Kalmijn J. The search for genes contributing to the low level of response to alcohol: Patterns of findings across studies. *Alcoholism: Clinical and Experimental Research*, 2004; 28(10):p1449-1458.

Secher M, Ritz P. Hydration and cognitive performance. *Journal of Nutrition Health and Aging*, 2012; 16(4):p325-329.

Sedman A, Wilkinson P, Sakmar E, Weidler D, Wagner J. Food effects on absorption and metabolism of alcohol. *Journal of Studies on Alcohol*, 1976; 37(9):p1197-1214.

Selzer M, Vinokur A, van Rooijen L. A self-administered short michigan alcoholism screening test (smast). *Journal of Studies on Alcohol*, 1975; 36(1):p117-126.

Serwah N, Marino F. The combined effects of hydration and exercise heat stress on choice reaction time. *Journal of Science and Medicine in Sport*, 2006; 9(1-2):p157-164.

Sharma V, Sridharan K, Pichan G, Panwar M. Influence of heat-stress induced dehydration on mental functions. *Ergonomics*, 1986; 29(6):p791-799.

Sharp R. Role of sodium in fluid homeostasis with exercise. *Journal of American College of Nutrition*, 2006; 25(3 Suppl):p231-239.

Sher K. Subjective effects of alcohol: The influence of setting and individual differences in alcohol expectancies. *Journal of Studies on Alcohol*, 1985; 46(2):p137-146.

Shillito M, King L, Cameron C. Effects of alcohol on choice reaction time. *Quarterly Journal of Studies on Alcohol*, 1974; 35(3):p1023-1034.

Shinar D. *Driver information processing: Attention, perception, reaction time and comprehension*. In Traffic safety and human behavior; 2007. Amsterdam, ND: Elsevier.

Shirreffs S. Markers of hydration status. *The Journal of Sports Medicine and Physical Fitness*, 2000; 40(1):p80-84.

Shirreffs S. Symposium on 'performance, exercise and health' hydration, fluids and performance. *Proceedings of the Nutrition Society*, 2009; 68(1):p17-22.

Shirreffs S, Maughan R. Restoration of fluid balance after exercise-induced dehydration: Effects of alcohol consumption. *Journal of Applied Physiology*, 1997; 83(4):p1152-1158.

Shirreffs S, Merson S, Fraser S, Archer D. The effects of fluid restriction on hydration status and subjective feelings in man. *British Journal of Nutrition*, 2004; 91(6):p951-958.

Shultz J, Weiner H, Westcott J. Retardation of ethanol absorption by food in the stomach. *Journal of Studies on Alcohol*, 1980; 41(9):p861-870.

Siegel S. Drug anticipation and drug addiction. The 1998 h. David archibald lecture. *Addiction*, 1999; 94(8):p1113-1124.

Siegel S. Drug tolerance, drug addiction, and drug anticipation. *Current Directions in Psychological Science*, 2005; 14(6):p296-300.

Simpson G. Do breath tests really underestimate blood alcohol concentration? *Journal of Analytical Toxicology*, 1989; 13(2):p120-123.

Smith M, Newell A, Baker M. Effect of acute mild dehydration on cognitive-motor performance in golf. *Journal of Strength and Conditioning Research*, 2012; 26(11):p3075-3080.

Solera A, Salazar W, Passe D. Influence of dehydration and rehydration on cognitive processes. *Medicine and Science in Sports and Exercise*, 1999; 31(5 Suppl):p905.

Southgate H. The effect of alcohol, under varying conditions of diet, on man and animals, with some observations on the fate of alcohol in the body. *The Biochemical Journal*, 1925; 19(5):p737-745.

Spaanjaars N, Spijkerman R, Engels R. Do smooth waters run deep? Alcohol intoxication and the effects of water consumption on driving-related cognitions and behavior. *European Addiction Research*, 2010; 17(1):p21-28.

Stewart J, de Wit H, Eikelboom R. Role of unconditioned and conditioned drug effects in the self-administration of opiates and stimulants. *Psychological Review*, 1984; 91(2):p251-268.

Stip E, Lecardeur L, Sepehry A. Computerised assessment of visuo-spatial cognition in schizophrenia: An exploratory meta-analysis of cantab findings. *European Psychiatric Review*, 2008; 1:p48-54.

Strauss A, Corbin J. *Basics of qualitative research: Techniques and procedures for developing grounded theory* (2 ed.); 1998. Thousand Oaks, California, USA: SAGE Publications Inc.

Strayer D, Drews F, Crouch D. A comparison of the cell phone driver and the drunk driver. *Human Factors*, 2006; 48(2):p381-391.

Stritzke W, Patrick C, Lang A. Alcohol and human emotion: A multidimensional analysis incorporating startle-probe methodology. *Journal of Abnormal Psychology*, 1995; 104(1):p114-122.

Sullivan E. Compromised pontocerebellar and cerebellothalamocortical systems: Speculations on their contributions to cognitive and motor impairment in nonamnesic alcoholism. *Alcoholism: Clinical and Experimental Research*, 2003; 27(9):p1409-1419.

Szinnai G, Schachinger H, Arnaud M, Linder L, Keller U. Effect of water deprivation on cognitive-motor performance in healthy men and women. *American Journal of Physiology: Regulatory, Integrative and Comparative Physiology*, 2005; 289(1):p275-280.

Taivainen H, Laitinen K, Tahtela R, Kilanmaa K, Valimaki M. Role of plasma vasopressin in changes of water balance accompanying acute alcohol intoxication. *Alcoholism: Clinical and Experimental Research*, 1995; 19(3):p759-762.

Taylor S, Chermack S. Alcohol, drugs and human physical aggression. *Journal of Studies on Alcohol*, 1993; 11(1 Suppl):p78-88.

Testa M, Collins L. Alcohol and risky sexual behavior: Event-based analyses among a sample of high-risk women. *Psychology of Addictive Behaviors*, 1997; 11(3):p190-201.

Testa M, Fillmore M, Norris J, Abbey A, Curtin J, Leonard K, Mariano K, Thomas M, Nomensen K, George W, VanZile-Tamsen C, Livingston J, Saenz C, Buck P, Zawacki T, Parkhill M, Jacques A, Hayman L. Understanding alcohol expectancy effects: Revisiting the placebo condition. *Alcoholism: Clinical and Experimental Research*, 2006; 30(2):p339-348.

Thompson R. The thermodynamics of drunk driving. *Journal of Chemical Education*, 1997; 74(5):p532-536.

Tiplady B, Franklin N, Scholey A. Effect of ethanol on judgments of performance. *British Journal of Psychology*, 2004; 95(1):p105-118.

Tiplady B, Oshinowo B, Thomson J, Drummond G. Alcohol and cognitive function: Assessment in everyday life and laboratory settings using mobile phones. *Alcoholism: Clinical and Experimental Research*, 2009; 33(12):p2094-2102.

Tomporowski P. Effects of acute bouts of exercise on cognition. *Acta Psychologica*, 2003; 112(3):p297-324.

Tomporowski P, Beasman K, Ganio M, Cureton K. Effects of dehydration and fluid ingestion on cognition. *International Journal of Sports Medicine*, 2007; 28(10):p891-896.

Törnros J. Driving behaviour in a real and a simulated road tunnel: A validation study. *Accident Analysis and Prevention*, 1998; 30(4):p497-503.

Transport: Roads and Maritime Services. *Road users' handbook*. NSW Government, 2012.

Vakulin A, Baulk S, Catcheside P, Anderson R, Van Den Heuvel C, Banks S, McEvoy R. Effects of moderate sleep deprivation and low-dose alcohol on driving simulator performance and perception in young men. *Sleep*, 2007; 30(10):p1327-1333.

Vakulin A, Baulk S, Catcheside P, Antic N, Van Den Heuvel C, Dorrian J, McEvoy R. Effects of alcohol and sleep restriction on simulated driving performance in untreated patients with obstructive sleep apnea. *Annals of Internal Medicine*, 2009; 151(7):p447-455.

Valenzuela C. Alcohol and neurotransmitter interactions. *Alcohol Health and Research World*, 1997; 21(2):p144-148.

Van Dongen H, Dinges D. *Circadian rhythms in fatigue, alertness and performance*. In Kryger M, Roth T, Dement W (Eds.), Principles and practice of sleep medicine; 2000 (3 ed.). Philadelphia, PA: W.B. Saunders.

Vanakoski J, Mattila M, Seppälä T. Driving under light and dark conditions: Effects of alcohol and diazepam in young and older subjects. *European Journal of Clinical Pharmacology*, 2000; 56(6-7):p453-458.

Veldstra J, Brookhuis K, de Waard D, Molmans B, Verstraete A, Skopp G, Jantos R. Effects of alcohol (bac 0.5%) and ecstasy (mdma 100 mg) on simulated driving performance and traffic safety. *Psychopharmacology*, 2011; 222(3):p377-390.

Verster J, Roth T. Standard operation procedures for conducting the on-the-road driving test, and measurement of the standard deviation of lateral position (sdlp). *International Journal of General Medicine*, 2011; 4:p359-371.

Vestal R, McGuire E, Tobin J, Andres R, Norris A, Mezey E. Aging and ethanol metabolism. *Clinical Pharmacology and Therapeutics*, 1977; 21(3):p343-354.

Vogel-Sprott M. *Alcohol tolerance and social drinking: Learning the consequences* (Vol. 15); 1992. New York: Guilford Press.

Vogel-Sprott M, Barrett P. Age, drinking habits and the effects of alcohol. *Journal of Studies on Alcohol*, 1984; 45(6):p517-521.

Volkow N, Mullani N, Gould L, Adler S, Guynn R, Overall J, Dewey S. Effects of acute alcohol intoxication on cerebral blood flow measured with pet. *Psychiatry Research*, 1988; 24(2):p201-209.

Wald J, Liu L. Psychometric properties of the drivr: A virtual reality driving assessment. *Studies in Health Technology and Informatics*, 2001; 81:p564-566.

Walker S, Ackland T, Dawson B. The combined effect of heat and carbon monoxide on the performance of motorsport athletes. *Comparative Biochemistry and Physiology Part A: Molecular & Integrative Physiology*, 2001; 128(4):p709-718.

Warren J. The effect of pure alcohol on the reaction time, with a description of a new chronoscope. *The Journal of Physiology*, 1887; 8(6):p311-348.

Watson P, Watson I, Batt R. Total body water volumes for adult males and females estimated from simple anthropometric measurements. *American Journal of Clinical Nutrition*, 1980; 33(1):p27-39.

Watson P, Watson I, Batt R. Prediction of blood alcohol concentrations in human subjects. Updating the widmark equation. *Journal of Studies on Alcohol*, 1981; 42(7):p547-556.

Watson W, Little H. *Alcohol and the brain*. In Caan W, De Belleroche J (Eds.), Drink, drugs and dependence: From science to clinical practice; 2002 (p39-50). London, UK: Routledge.

Weafer J, Fillmore M. Acute tolerance to alcohol impairment of behavioral and cognitive mechanisms related to driving: Drinking and driving on the descending limb. *Psychopharmacology*, 2011; 220(4):p697-706.

Weissenborn R, Duka T. Acute alcohol effects on cognitive function in social drinkers: Their relationship to drinking habits. *Psychopharmacology*, 2003; 165(3):p306-312.

Welling P, Lyons L, Elliott R, Amidon G. Pharmacokinetics of alcohol following single low doses to fasted and nonfasted subjects. *Journal of Clinical Pharmacology*, 1977; 17(4):p199-206.

251

West R, Wilding J, French D, Kemp R, Irving A. Effect of low and moderate doses of alcohol on driving hazard perception latency and driving speed. *Addiction*, 1993; 88(4):p527-532.

Wester A, Verster J, Volkerts E, Böcker K, Kenemans J. Effects of alcohol on attention orienting and dual-task performance during simulated driving: An event-related potential study. *Journal of Psychopharmacology*, 2010; 24(9):p1333-1348.

Westerfeld W. The intermediary metabolism of alcohol. *The American Journal of Clinical Nutrition*, 1961; 9:p426-431.

Westgard J, Hunt M. Use and interpretation of common statistical tests in method-comparison studies. *Clinical Chemistry*, 1973; 19(1):p49-57.

Wewers M, Lowe N. A critical review of visual analogue scales in the measurement of clinical phenomena. *Research in Nursing & Health*, 1990; 13(4):p227-236.

Whitfield J. Adh and aldh genotypes in relation to alcohol metabolic rate and sensitivity. *Alcohol and Alcoholism*, 1994; 2:p59-65.

Whitfield J, Martin N. Alcohol consumption and alcohol pharmacokinetics: Interactions within the normal population. *Alcoholism: Clinical and Experimental Research*, 1994; 18(2):p238-243.

Widmark E. *Principles and applications of medicolegal alcohol determination*; 1981. Biomedical Publications.

Wiese J, Shlipak M, Browner W. The alcohol hangover. *Annals of Internal Medicine*, 2000; 132(11):p897-902.

Williams R, Goldman M, Williams D. Expectancy and pharmacological effects of alcohol on human cognitive and motor performance: The compensation for alcohol effect. *Journal of Abnormal Psychology*, 1981; 90(3):p267-270.

Wilson M, Morley J. Impaired cognitive function and mental performance in mild dehydration. *European Journal of Clinical Nutrition*, 2003; 57(2 Suppl):p24-29.

Winek C, Carfagna M. Comparison of plasma, serum, and whole blood ethanol concentrations. *Journal of Analytical Toxicology*, 1987; 11(6):p267-268.

World Health Organisation. *Drinking and driving: A road safety manual for decision-makers and practitioners*. Global Road Safety Partnership, Geneva; 2007.

Wyon D, Wyon I, Norin F. Effects of moderate heat stress on driver vigilance in a moving vehicle. *Ergonomics*, 1996; 39(1):p61-75.

Yelland L, Burns J, Sims D, Salter A, White J. Inter- and intra-subject variability in ethanol pharmacokinetic parameters: Effects of testing interval and dose. *Forensic Science International*, 2008; 175(1):p65-72.

Yun D, Hwang S, Kim Y, Lee Y, Kim Y, Jung H. Impairments in executive functioning in patients with remitted and non-remitted schizophrenia. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, 2011; 35(4):p1148-1154.

Zador P, Krawchuk S, Moore B. *Drinking and driving trips, stops by the police, and arrests: Analyses of the 1995 survey of drinking and driving attitudes and behavior*. National Highway Traffic Safety Administration, Washington, DC; 2000.

Zhang Z, Snizek W. Occupation, job characteristics, and the use of alcohol and other drugs. *Social Behavior and Personality*, 2003; 31(4):p395-412.

Zuba D. Accuracy and reliability of breath alcohol testing by handheld electrochemical analysers. *Forensic Science International*, 2008; 178:p29-33.

Zuckerman M. *Behavioral expressions and biosocial bases of sensation seeking*; 1994. Cambridge University Press.

Zuri R, Cleary M, Lopez R, Jones L, Moseley B. Cognitive performance may be impaired by exercise in hot, humid environment: A preliminary investigation. *3rd Annual College of Education Research Conference,* 2004; Florida International University, Miami, Florida USA, p128-133.