Title:

The effects of dehydration, moderate alcohol consumption, and rehydration on cognitive functions

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Abstract

This study investigated the impact of mild-moderate dehydration on alcohol-induced deteriorations in cognitive functions. Sixteen healthy males participated in a single-blind, placebo-controlled cross-over design study involving 4 experimental trials (separated by ≥ 7 d). In each trial, participants were dehydrated by 2.5% body mass through exercise. After 1 h recovery in a thermo-neutral environment ($22 \pm 2^\circ\text{C}$, 60-70% relative humidity) 4 tasks from the Cambridge Neuropsychological Test Automated Battery (CANTAB) were administered to the participants (test 1). In two of the trials, participants were provided with water equivalent to either 50% or 150% body mass loss and given salt (NaCl) capsules (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 same 4 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. Alcohol consumption caused deterioration on 3 of the 4 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. 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.

Key Words: Ethanol, Hypohydration, Rehydration, Cognitive Performance

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 and 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 and Fiorentino, 2000; Moskowitz and Robinson, 1988); choice reaction time (Moskowitz and Fiorentino, 2000); response inhibition to stop-signal and go/no-go tasks (de Wit et al., 2000; Fillmore, 2007; Marcinski et al., 2005); and tasks associated with executive function such as the Tower of London or Stockings of Cambridge Test that involve spatial planning and motor control (Weissenborn and 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 and Robinson, 1988) and the effects are obvious at high ($>0.10\%$) blood alcohol concentrations (BACs). Inconsistencies are reported in the literature with low ($<0.05\%$) to moderate ($0.05\text{--}0.10\%$) levels of alcohol intoxication (Ogden and 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 and 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 Cambridge Neuropsychological Automated Testing Battery (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 (Tower of London Task/Stockings of Cambridge) 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; Fillmore, 2007; Marcinski et al., 2005). 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 and 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 and 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., 2001; Cian et al., 2000) 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 and Sawka, 2007). However, most studies induce dehydration through exercise methods in warm environments (Grandjean and Grandjean, 2007) and relatively few have investigated the effects of dehydration on cognitive performance independent of an applied heat stress (Cian et al., 2001; Cian et al., 2000).

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 and 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., 2011; Kempton et al., 2009).

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 individuals' ability to carry out everyday tasks such as driving a motor vehicle or operating machinery.

The aim of the present 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.

Materials and Methods

Participants

Sixteen healthy untrained males (22.7 ± 3.3 y, 77.28 ± 9.13 kg body weight (BW), 176.7 ± 5.7 cm, VO_2 peak 43.0 ± 4.7 ml/kg/min; values are mean $\pm$ SD) volunteered to participate in the present study. Participants had a regular history of alcohol consumption of 5.2 ± 3.7 y. 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 10 g 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 the Human Research Ethics Committee of Griffith University (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 5 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 5 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 practiced each of the cognitive tasks until they were comfortable with the procedures.

Experimental design

Each participant undertook four experimental trials (Fig. 1). The trials were completed using a single-blind administration protocol and the four experimental treatments were randomised via an incomplete Latin square design.

Pre-Experimental Procedures

Experimental trials were separated by at least 7 days and were conducted at the same time of the day in a stable laboratory environment ($22\pm 2^\circ\text{C}$, 60-70% relative humidity). Participants were asked to abstain from alcohol for 24 h, and caffeine-containing substances and moderate-strenuous exercise for 12 h prior to each experimental trial. During the 24 h 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 ~0700-0800 h. Compliance to pre-experimental conditions was verbally acknowledged on arrival and a measure of breath alcohol concentration (BrAC) was taken to verify a zero alcohol reading. A urine sample was then collected to calculate urine specific gravity (U_{sg}) as an initial measure of hydration status. Participants that 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. 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 (Accucheck 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 and 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, 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 1 min 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_i and nude body weight was recorded, before participants had a cool shower. After the shower, participants dried themselves thoroughly and a nude body mass measurement was made before they rested for a period of 1 h. At the end of the recovery period, a second MRS was completed and measures of T_i and BGL were recorded.

Following the recovery period, 4 tasks from the Cambridge Neuropsychological Test Automated Battery (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) made up with equal parts of non-alcoholic diet ginger beer cordial concentrate (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). 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 identical to the alcoholic drink however water was substituted for vodka. A pilot study involving 34 participants was completed earlier to

design and confirm the credibility of the placebo beverage by comparing ratings of taste and other sensory properties between the drinks. In the present study, participants were not informed of a placebo trial and were under the expectancy of receiving alcohol in all trials. A mist of vodka was sprayed over the placebo beverage and on the rim of the container to provide olfactory cues similar to that of the alcohol containing beverage. 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 drinks were rated by perceived alcohol concentration (no alcohol, low alcohol, moderate alcohol, high alcohol) and certainty of perception (not at all certain, somewhat certain, very certain, absolutely certain) using 4-point Likert scales.

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 differentiated by $\geq 0.005\%$. 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, the same 4 tasks from the CANTAB were administered (test 2) before a final BrAC, urine volume and body weight was recorded (~60 min post ingestion). At the end of the trial, participants were provided with snacks and drinks, and given taxi vouchers to ensure safe transportation home.

Cognitive tasks (CANTAB)

Assessment of cognitive performance was completed using a 4-task CANTAB test battery. Many studies support the validity and use of neuropsychological assessment with the CANTAB (Egerhazi et al., 2007; Fowler et al., 1997; Fray and Robbins, 1996; Lange et al., 1992; Louis et al., 1999; Robbins et al., 1998; Robbins et al., 1994; Weissenborn and Duka, 2003). 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; Friedman et al., 2010; Weissenborn and Duka, 2003), and to examine cognitive domains that are likely to be relevant to driving related skills.

Participants completed the following tests, which were administered for each trial 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).

Subjective ratings

Adaptive Visual Analogue Scales (AVAS) were used to assess mood (Bond and 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 (Dell Latitude, E5400).

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 and 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; Fillmore et al., 2008; Harrison et al., 2007).

Statistical analysis

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 and test 2 responses for each trial. Comparisons between trials were conducted using one-way repeated-measures analysis of variance (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 ($P < .05$). 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 $P < .05$. All data are reported as mean $\pm$ standard deviation unless otherwise specified.

Results

Cognitive performance measures

Choice Reaction Time (CRT). A significant increase in latency was observed for DA and PA trials ($P < .05$) with no differences noted between the tests for both DP and FA trials (Fig. 2a). The percentage of correct responses showed no significant variation between tests regardless of trial conditions (Fig. 2b). Participants had a high degree of success ($>98\%$ correct) in response selection to stimuli across both testing stages in all trials.

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 ($P > 0.05$) (Fig. 2c and 2d). 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 ± 454 msec). Mean movement time was 460 ± 176 msec and the proportion of correct responses was high ($93.2 \pm 6.4\%$) across all trial conditions. This task was not sensitive to the conditions employed across trials in this study.

Stop Signal Task (SST). Differences in stop-signal reaction time (SSRT) and number of direction errors made are illustrated in Fig. 2e and Fig. 2f respectively. There was a significant difference in SSRT between tests for the DA trial, with a slower response recorded after ingestion of alcohol ($P < .05$). No difference was seen in any of the other conditions ($P > .05$). There was no difference between tests for the proportion of successful stops made in any of the trials ($P > .05$). Significantly more direction errors were made during test 2 for both DA and FA trials compared to test 1 ($P < .05$).

Stockings of Cambridge (SOC). A significant difference in the number of problems solved in minimum number of moves was observed for the FA trial ($P < .05$) with no differences between tests in any of the other trials (Fig. 2g). 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 $n = 5$ moves task was observed in test 2 of the FA trial (Fig. 2h). No differences were recorded for the $n = 5$ move task in any other trials ($P > .05$).

Mood rating

A number of significant effects were found on measures derived from the MRS questionnaires (Fig. 3). On the alert-drowsy scale, there was a significant main effect for time, $F(2,30)=4.23$; $P=.024$, but no effect of protocol, $F(3,45)=1.20$; $P=.322$, or protocol x time interaction, $F(6,90)=0.59$, $P=.740$. Post hoc analysis revealed higher ratings of drowsiness at time 3 compared to time 1 ($P < .05$). For the confused-clear headed scale, there was a significant main effect for time, $F(2,30)=14.18$; $P < .001$, with higher ratings of confusion at each subsequent time point ($P < .05$), but no effect of protocol, $F(3,45)=1.56$; $P=.212$, or protocol x time interaction, $F(6,90)=1.58$; $P=.163$. On the well coordinated-clumsy scale, there was a significant main effect for both protocol, $F(3,45)=3.38$; $P=.026$, and time, $F(2,30)=16.38$; $P < .001$, but no protocol x time interaction, $F(6,90)=1.49$; $P=.192$. Post hoc analysis revealed higher levels of clumsiness at each subsequent time point and on all alcohol trials compared to the placebo trial ($P < .05$). For the incompetent-competent scale, there was a significant main effect for time, $F(2,30)=8.48$; $P=.001$, with higher levels of incompetence reported at time 2 and 3 compared to time 1 ($P < .05$), but no effect of protocol, $F(3,45)=0.18$; $P=.909$, or protocol x time interaction, $F(6,90)=1.92$; $P=.087$.

There were no significant main effects of protocol, $F(3,45)=1.003$; $P=.400$, time, $F(2,30)=2.69$; $P=.084$, or protocol x time interaction, $F(6,90)=0.305$; $P=.933$, 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, $F(3,45)=1.79$; $P=.164$, time, $F(2,30)=3.13$; $P=.058$, or protocol x time interaction, $F(6,90)=1.97$; $P=.079$, indicating that trial results were not influenced by boredom.

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.

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. 4). Ratings for the placebo trial were significantly lower than alcohol trials ($P<.05$), 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 ($P<.05$).

Levels of hydration and body mass changes

The dehydration protocol was successful in achieving similar levels of body mass loss between trials (Table 1). Significant differences in body mass were recorded between trials after rehydration ($P<.05$). These differences remained significant with the final body weight measurement taken after CANTAB test 2 ($P<.05$).

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. Urine output was measured at hourly intervals from the start of the rehydration protocol. The cumulative urine volumes for each trial produced over the three hours are shown in Fig. 5. A significantly greater urine output was measured for the FA trial compared to all other trials ($P<.05$). There was no difference in urine output between the two dehydration trials (DP and DA) and the PA trial ($P>.05$).

Physiological measures

Summary data for physiological measures taken throughout testing are presented in Table 2. Tympanic temperature increased significantly with exercise ($P<.05$). 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 ($P<.05$), however the differences were not considered clinically significant and were within the error margins indicated for accuracy of the tympanic device ($\pm 0.2^\circ\text{C}$). 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 ($P\leq.05$). However values recorded on final measures

taken prior to CANTAB test 2 were still within the accepted range for normal glycemia (Diabetes Australia, 2009).

Breath alcohol concentrations (BrACs)

No significant difference in BrAC was recorded between trials at any of the measured time points ($P < .05$). Peak BrACs were achieved 15-30 min post alcohol ingestion with mean levels of $0.072 \pm 0.017\%$, $0.074 \pm 0.017\%$, and $0.072 \pm 0.015\%$ for the DA, PA and FA trials respectively. As expected, no measurable breath alcohol was detected for the DP trial (Fig. 6). 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 ($0.063 \pm 0.009\%$, $0.064 \pm 0.005\%$, and $0.060 \pm 0.006\%$ for DA, PA, and FA trials respectively) noted in all trials ($P < .05$).

Discussion

To our knowledge the present investigation is the first 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 the present study indicate that mild to moderate dehydration causes greater deterioration of some cognitive functions in individuals that 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 in regard to the number of correct responses made. Alcohol administration in doses that elicit concentrations

above 0.06% have shown consistent impairing effects on CRT tasks in previous research (Maylor and Rabbitt, 1993; Moskowitz and Fiorentino, 2000). However, studies specifically investigating the impact of dehydration on CRT tasks have typically not found effects (Armstrong et al., 2010; Cian et al., 2001; Cian et al., 2000; D'Anci et al., 2009; McMorris et al., 2006; Neave et al., 2001; Serwah and Marino, 2006; Szinnai et al., 2005) 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 on 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., 2001; Cian et al., 2000). 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 and Maltzman, 1991; Weissenborn and 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., 2010). 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 and 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 (Heishman et al., 1997; Lex et al., 1988; 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 and 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 (Hull and Bond, 1986; Stewart et al., 1984) 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 a 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.

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Tables

Table 1. Mean percentage of body mass 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	$-1.54 \pm 0.27^*$	$-1.41 \pm 0.38^*$
FA	-2.47 ± 0.29	$+0.19 \pm 0.49^*$	$-0.56 \pm 0.63^*$

DP, dehydration-placebo trial; DA, dehydration-alcohol trial; PA, partial rehydration-alcohol trial; FA, full rehydration-alcohol trial. *Significant difference from all other trials. Values are mean $\pm$ SD.

Table 2. 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	$37.1 \pm 0.5^{**}$	$37.1 \pm 0.5^{**}$	$37.2 \pm 0.5^{**}$	$37.2 \pm 0.5^{**}$
CANTAB (test1)	$36.4 \pm 0.3^*$	36.3 ± 0.4	$36.3 \pm 0.5^*$	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)	$5.6 \pm 0.5^{**}$	$5.5 \pm 0.5^*$	$5.7 \pm 0.5^{**}$	$5.5 \pm 0.5^{**}$

DP, dehydration-placebo trial; DA, dehydration-alcohol trial; PA, partial rehydration-alcohol trial; FA, full rehydration-alcohol trial. ^{*}Significant difference from pre-trial measures ($P \leq 0.05$). ^{**}Significant difference from pre-trial and CANTAB (test 1) measures ($P < .05$). Values are mean $\pm$ SD.

Figure Captions

Fig. 1. 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 VAS and SIIS refers to the administration of the subjective intoxication and impairment scale VAS. Drink corresponds to rehydration trials where 50% (P, partial) or 150% (F, full) of fluid loss is replaced.

Fig. 2. (a) CRT mean reaction time, (b) CRT response accuracy, (c) MTS mean correct reaction time, (d) MTS response accuracy, (e) SST mean SSRT, (f) SST mean number of direction errors, (g) SOC mean number of problems solved in minimum moves, (h) SOC mean number of moves required to complete the $n=5$ move task. DP, dehydration-placebo trial; DA, dehydration-alcohol trial; PA, partial rehydration-alcohol trial; FA, full rehydration-alcohol trial; T1, CANTAB test 1; T2, CANTAB test 2. *Significant difference between T1 and T2 results ($P<.05$). Values are mean $\pm$ SEM.

Fig. 3. Mood Rating Scale VAS scores. Alert - Drowsy, Confused - Clear-Headed, Well-Coordinated - Clumsy, Incompetent - Competent, Lethargic - Energetic, Interested - Bored. DP, dehydration-placebo trial; DA, dehydration-alcohol trial; PA, partial rehydration-alcohol trial; FA, full rehydration-alcohol trial. *Significant difference between times, protocols, or trials; see text for details ($P<.05$). Values are mean $\pm$ SD.

Fig. 4. Subjective ratings of alcohol effects, level of impairment, ability to drive and willingness to drive a car for each trial. DP, dehydration-placebo trial; DA, dehydration-alcohol trial; PA, partial rehydration-alcohol trial; FA, full rehydration-alcohol trial. *Significant difference compared to placebo trial ($P<.05$). Values are mean $\pm$ SD.

Fig. 5. Total fluid intake and cumulative urine volume produced on each trial. DP, dehydration and placebo; DA, dehydration and alcohol; PA, partial rehydration and alcohol; FA, full rehydration and alcohol. *Significant difference compared to all trials ($P<.05$). Values are mean $\pm$ SD.

Fig. 6. 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. *Significant difference from BrAC at time 30min ($P<.05$). Values are mean $\pm$ SD.