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A Mixed Hazard:

Co-Ingesting Alcohol and Energy Drinks and the Associated Harms

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Submitted in fulfilment of the requirements for the Degree of

Doctor of Philosophy

School of Psychology, University of Tasmania

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Declaration of Originality

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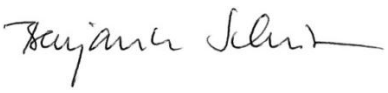
Signed:  

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Abstract

Alcohol mixed with energy drinks (AmED) is an increasingly popular consumption trend generating concern amongst researchers, health professionals, and policy-makers. It has been theorised that the stimulant effects of the energy drink (ED) mask the depressant outcomes of alcohol, causing reduced perception of intoxication, and increased alcohol-related harms, particularly in regards to behavioural risk-taking. Despite calls for further marketing and sales regulation, there is a lack of research investigating the consumption patterns, motivations for, and consequences of, AmED use, particularly for consumers in the general community. Key gaps in the current literature relate to the paucity of: (i) within-subject research assessing intoxication outcomes after AmED versus alcohol to determine whether consumers experience additional alcohol-related harms from co-ingestion, and (ii) experimental laboratory-based controlled research objectively assessing AmED and alcohol intoxication outcomes to examine the pharmacological effects of co-ingestion.

The aim of this thesis was to address some of these limitations. A systematic review of the literature examining the physiological, psychological, and behavioural harms of AmED versus alcohol use was conducted. Three studies were also undertaken: (1) an online survey of community-based Australians identifying as AmED consumers (*N*=403) assessing AmED consumption patterns and motivations for use, as well as the physiological, psychological, and behavioural consequences of AmED versus alcohol use, (2) a single-blind, placebo-controlled crossover experimental study (*N*=28) assessing the effect of an acute alcohol (target breath alcohol concentration

(BrAC) .050%) and ED (3.57mL/kg; approximately one standard 250mL ED per 70kg person) dose on subjective measures of physiological and psychological intoxication, and objective measures of risk-taking and impulsive behaviour, and (3) a single-blind, placebo-controlled, mixed design experimental study (*N*=30) assessing the dose-dependent effects of acute alcohol (placebo, target BrAC .050%, and .080%) and ED (placebo, 250mL, 500mL, and 750mL) administration on objective and subjective intoxication.

In *Study 1*, only one-fifth of the sample reported potentially harmful motives for AmED use related to increasing alcohol intake, altering alcohol-induced impairment, or seeking a 'high' similar to illicit drugs. However, participants reported typically exceeding Australian recommended maximum intake guidelines for both independent constituents in AmED drinking sessions, as well as late-night initiation of use in licensed venues. This excess intake was particularly concerning considering the physiological and psychological intoxication profile reported in *Study 1*, with increased odds of stimulation-based outcomes (e.g., heart palpitations, sleeping difficulties, tension), as well as decreased odds of sedation-based outcomes which might signal to the consumer their level of intoxication (e.g., speech and walking difficulties), during AmED versus alcohol drinking sessions. This change to the nature of intoxication was generally not apparent in the experimental research, with little evidence of interactive subjective AmED effects in a controlled setting in *Study 2*, potentially attributable to the discrepancy between low experimental dosing and self-reported excess real-life intake.

In contrast with predictions, participants in *Study 1* retrospectively self-reported lower odds of risk-taking in AmED versus alcohol drinking sessions. Similarly, the experimental research showed that alcohol-induced increased impairment in one aspect of impulsive behaviour, impulsive response initiation (assessed via the Immediate Memory/Delayed Memory Task), was reduced following ED co-ingestion. This effect was specific to the delayed memory component of the task; no interactive effects of alcohol and ED were evident for the immediate memory component, or for performance on a measure of response disinhibition, the Cued Go/No-Go task, or a measure of impulsive decision-making, the Experiential Discounting Task. However, a significant, yet small magnitude, increase in objectively-measured risk-taking, assessed via the Balloon Analogue Risk Task, was apparent following ED administration, regardless of the presence or absence of alcohol.

Despite this limited support for theorised AmED-induced increases in risk-taking, the final experimental study reinforced the premise of reduced perception of intoxication post-AmED consumption. Decreases in perceived intoxication were evident only after co-ingesting a moderate alcohol dose (target BrAC .050%) with 750mL ED, a dose which exceeded the Australian maximum recommended daily intake guideline (i.e., two standard 250mL ED serves containing 80mg caffeine per serve). This effect was apparent after accounting for ED-related dose-dependent decreases in BrAC.

Overall, this research suggests that AmED consumption may alter the nature and intensity of intoxication in a manner which has the potential to increase the risk of

adverse alcohol-related outcomes. However, conflicting evidence is provided as to whether additional pharmacologically-derived behavioural harms are apparent following AmED use: consumer self-report indicated lower levels of risk-taking, whilst laboratory-based objective measurement typically showed no appreciable change or decreased alcohol-induced elevation of impulsive behaviour after AmED, as well as small magnitude increases in risky behaviour after AmED (although this effect occurred after ED administration in general). Clarification as to the relative contribution of pharmacological (e.g., dose) and non-pharmacological (e.g., psychological, personality, and environmental) factors in future research would strengthen this foundational evidence base to determine appropriate harm reduction public health reform approaches.

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Chapter 3: **Peacock, A.,** Bruno, R., & Martin, F. (2013). Patterns of use and motivations for consuming alcohol mixed with energy drinks. *Psychology of Addictive Behaviors, 27,* 202-206.

Chapter 4: **Peacock, A.,** Bruno, R., & Martin, F. (2012). The subjective physiological, psychological, and behavioral risk-taking consequences of alcohol and energy drink co-ingestion. *Alcoholism: Clinical and Experimental Research, 36,* 2008-2015.

Chapter 6: **Peacock, A.,** Bruno, R., Martin, F., & Carr, A. (2013). The impact of alcohol and energy drink consumption on intoxication and risk-taking behavior. *Alcoholism: Clinical and Experimental Research, 37,* 1234-1242.

Appendix D: **Peacock, A.,** Bruno, R., & Martin, F. (2013). Valid points but the trends remain: A response to Rossheim, Suzuki, and Thombs. *Alcoholism: Clinical and Experimental Research, 37,* 2171-2174.

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Chapter 5: **Peacock, A.,** Bruno, R., Martin, F., & Carr, A. (under review). Self-reported physiological and psychological side-effects of an acute alcohol and energy drink dose. *Appetite*.

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Peacock, A., Bruno, R., Martin, F., & Carr, A. Physiological and psychological outcomes of alcohol and energy drink co-ingestion. 36th Annual Research Society on Alcoholism Scientific Meeting, June 2013, Orlando, United States. Poster presentation.

Peacock, A., Bruno, R., Martin, F., & Carr, A. Subjective perception of intoxication following alcohol and energy drink consumption. Australasian Professional Society on Alcohol and other Drugs Conference, November, 2012, Melbourne, Australia. Poster presentation.

Peacock, A., Bruno, R., Martin, F., & Carr, A. The impact of independent and combined alcohol and energy drink consumption on risk-taking behaviour. Australasian Professional Society on Alcohol and other Drugs Conference, November, 2012, Melbourne, Australia. Oral presentation.

Peacock, A., Bruno, R., & Martin, F. Patterns of use and motivations for co-ingestion of alcohol mixed with energy drinks. 35th Annual Research Society on Alcoholism Scientific Meeting, June 2013, San Francisco, United States. Poster presentation.

Peacock, A., Bruno, R., & Martin, F. The subjective physiological, psychological, and behavioural risk-taking consequences of alcohol and energy drink co-ingestion. 35th Annual Research Society on Alcoholism Scientific Meeting, June 2013, San Francisco, United States. Poster presentation.

Peacock, A., Bruno, R., & Martin, F. Alcohol and energy drink co-ingestion: Motivations and consequences. Alcohol, Tobacco & other Drug Council Conference, May, 2012, Hobart, Australia. Oral presentation.

Peacock, A., Martin, F., & Bruno, R. Motivations for, and consequences of, energy drink and alcohol co-ingestion. Australasian Professional Society on Alcohol and other Drugs Conference, November, 2011, Hobart, Australia. Oral presentation.

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Chapter 1: Introduction

1.1 Theoretical Background

Alcohol consumption is responsible for considerable problems at an individual and population level, causing reduced workplace productivity and detrimental health effects, and contributing to antisocial, criminal, and violent behaviour (Laslett et al., 2010; Manning, Smith, & Mazerolle, 2013). The harms of alcohol consumption are particularly prevalent amongst adolescents and young adults due to elevated rates of high-risk drinking (Australian Institute of Health and Welfare, 2011). A new and increasingly prevalent consumption trend amongst young people, mixing alcohol with energy drinks (AmED), is generating considerable media interest and causing concern for regulatory bodies (Arria & O'Brien, 2011; Australian Medical Association, December, 2012; Weldy, 2010). Energy drinks (EDs) are beverages marketed as improving performance by reducing fatigue and increasing alertness (Heckman, Sherry, & de Mejia, 2010). The combination of alcohol and EDs can be achieved by purchasing pre-mixed beverages, hand-mixing the two constituents, or consuming the two beverages separately in a drinking session. Studies targeting adolescent and young adult samples, key risk groups for hazardous alcohol use, indicate that AmED use may feature as part of the repertoire of younger alcohol consumers, with up to three-quarters of university students reporting lifetime AmED use (L. Berger, Fendrich, Chen, Arria, & Cisler, 2011; Brache & Stockwell, 2011; O'Brien, McCoy, Rhodes, Wagoner, & Wolfson, 2008).

Concern regarding the prevalence of AmED use amongst young adults is partially founded on the motivations for use; primarily, an explicit intention to alter intoxication. Firstly, researchers have theorised that the sweet taste of EDs is used to create a beverage which is more palatable and masks the taste of alcohol, facilitating

intake (Arria et al., 2011). Secondly, it is theorised that consumers co-ingest ED to increase alertness and reduce sedation, facilitating a more desirable intoxication state which may allow the consumer to stay out later and continue alcohol consumption (Arria et al., 2011; Weldy, 2010). These motivations for use could result in high-risk consumption patterns, whereby consumers are ingesting excess quantities of AmED in the night-time economy.

The assumption of a stimulation-based intoxication state following AmED consumption is logical based on the stimulant and depressant pharmacological actions of ED and alcohol, respectively. The two constituents are thought to have oppositional global pharmacological effects, whereby the stimulatory nature of the ED masks the depressant effects of alcohol, causing a state of 'wide-awake drunkenness' (Arria & O'Brien, 2011). This state of intoxication may increase the risk of additional negative physiological and psychological stimulation-based side-effects relative to when alcohol is consumed alone. It may also mask those sedation-related effects (e.g., fatigue) which act as a subjective indicator of intoxication (Marczinski, Fillmore, Bardgett, & Howard, 2011). Consequently, AmED consumers may have a reduced ability to accurately perceive intoxication, underestimating their degree of inebriation relative to if they had consumed the same amount of alcohol without ED (Ferreira, de Mello, Pompeia, & de Souza-Formigoni, 2006).

Of particular concern, this misperception of intoxication may impact on accurate risk assessment. Specifically, consumers may display poorer decision-making, and increased risky and impulsive behaviour, as a consequence of perceiving their level

of intoxication as lower relative to when ingesting the same dose of alcohol without ED. This change in behaviour could heighten the risk of alcohol-related harm resulting from an overestimate of ability, including driving while intoxicated, engaging in disinhibited behaviour (e.g., physical and verbal abuse), or being injured from falls or accidents. It has been well-established that AmED consumers, relative to alcohol consumers, generally display greater risk-taking propensity whilst sober and intoxicated (e.g., Brache & Stockwell, 2011; O'Brien et al., 2008). This trait predisposition towards risk-taking, coupled with potential state-dependent increased risk-taking after AmED consumption, contribute towards a hypothesised high-risk profile of alcohol-related harms for this consumer group.

1.2 Rationale

AmED is a relatively new consumption trend; the body of research investigating this phenomenon is small despite a recent increase in interest. To date, there have been no major public health campaigns or legislative changes in Australia in relation to AmED use despite calls for reform (Australian Medical Association, December, 2010). Pennay and Lubman (2012b) argue that the impediment is the paucity of research at the community level investigating how people consume AmED; specifically, the amount, frequency, and context of use, and the motivations behind beverage choice. Those studies which have focused on the consumption patterns and motivations for AmED use have primarily sampled high-risk consumer subgroups (generally university students) in the United States, Canada, and Europe (e.g., L. Berger et al., 2011; de Haan, de Haan, van der Palen, Olivier, & Verster, 2012; Thombs et al., 2010; Woolsey, Waigandt, & Beck, 2010). To date, there has been no

systematic investigation of the consumption patterns and motivations for AmED use in the Australian community.

Pennay and Lubman (2012b) also claim that efforts towards regulating AmED sales and marketing are further undermined by a dearth of research investigating the causal link between AmED consumption and negative outcomes. The majority of studies in this field of research compare alcohol-related consequences for two consumer groups: AmED versus non-AmED consumers (L. Berger, Fendrich, & Fuhrmann, 2013; Miller, 2012; O'Brien et al., 2008; Penning, de Haan, & Verster, 2011; Snipes & Benotsch, 2013). These studies consistently indicate that AmED consumers experience more negative consequences of alcohol consumption than non-AmED consumers. However, a causal link between AmED consumption and negative physiological, psychological, and behavioural outcomes cannot be inferred from these studies. AmED consumers typically have a unique demographic and personality profile relative to non-AmED consumers, highlighted by their elevated innate tendency towards impulsive and risky behaviour (Brache & Stockwell, 2011). Comparing retrospective self-reported alcohol-related consequences of AmED versus alcohol consumption for the same individuals (within-subject comparison) circumvents this issue. However, there has only been one such study conducted to date (de Haan et al., 2012). In contrast with predictions outlined in Section 1.1., this study by de Haan et al. (2012) indicated that consumers retrospectively self-reported lower rates of alcohol-related consequences after AmED relative to alcohol consumption. This study focused only on the drinking experiences of European university students; to date, there have been no published attempts to replicate these

outcomes, nor has there been any research assessing whether these findings are reflected at the community-level or in other drinking cultures.

Self-report of drinking consequences can provide a comprehensive overview of alcohol-related outcomes over multiple drinking sessions. However, these reports can be influenced by biased reporting, particularly when consumers are asked to retrospectively recall events occurring within a lengthy time period (e.g., in the last year). Furthermore, alcohol-related consequences may not be exclusively attributed to the pharmacological effects of the beverage, as internal (e.g., drinking expectancies) and external (e.g., drinking environment) factors may play a role in the drinking experience. Laboratory-based testing of the acute effects of a blinded dose provides a more direct method of assessing the pharmacological effects of AmED, as the experimenter can control for these confounding variables. Outcomes can be objectively assessed using computer-based tasks, circumventing recall and self-presentation biases inherent in self-report. Despite the advantages of this research design, there has been no targeted controlled laboratory-based research conducted to date assessing whether physiological, psychological, and behavioural harms increase appreciably when AmED is consumed relative to alcohol. This dearth of research precludes any conclusions regarding the direct pharmacological effects of co-ingesting ED, leaving policy-makers with no solid empirical evidence base upon to support regulation of ED sold in conjunction with alcohol.

Focusing specifically on the potential behavioural outcomes of use, it has been well-established in past experimental research that alcohol causes state-dependent changes in behaviour, decreasing behavioural inhibition and increasing risky and

impulsive behaviour. In regards to the latter behavioural outcome, alcohol appears to exert a differential effect dependent upon the aspect of impulsive behaviour being assessed: impulsive response inhibition, response disinhibition, or impulsive decision-making (de Wit, 2009; Dougherty, Marsh, Hatzis, Nouvion, & Mathias, 2008). Despite previous research showing that stimulant co-ingestion can attenuate alcohol-induced increases in impulsive behaviour (e.g., Fillmore & Vogel-Sprott, 1999), there has been little research assessing the interactive effect of ED in combination with alcohol on the varying aspects of impulsive behaviour. To date, only one study has investigated the effect of AmED on response disinhibition, finding equivalent outcomes regardless of whether ED was co-ingested with alcohol or not (Marczinski et al., 2011); the relative effect of AmED versus alcohol on each of these aspects of impulsive behaviour has not been examined concurrently.

However, the aforementioned shortcomings within this body of literature are overshadowed by one major oversight, the outcomes of which could alter the methodological and analytical approach adopted when comparing the relative effects of AmED versus alcohol ingestion. The theorised changes in consumption patterns, motivations for, and consequences of, AmED use are generally attributed to AmED-induced reduced perception of intoxication. For this premise to hold true, subjective ratings of intoxication should be lower after AmED versus alcohol consumption, whilst objective intoxication outcomes (e.g., BrAC) remain comparable. In contrast with predictions, the few experimental studies directly assessing objective and subjective intoxication in experimental settings have yielded equivalent outcomes following AmED and alcohol administration (Marczinski et al., 2011; Marczinski, Fillmore, Henges, Ramsey, & Young, 2012, 2013). These studies have generally

involved administration of a dose equivalent to a single standard 250mL ED (per 70kg person), a lower amount relative to that typically ingested in real-life AmED drinking sessions (Woolsey et al., 2010). This focus on low and simple dosing protocols contributes to the initial development of an evidence-base regarding the relative effects of AmED versus alcohol consumption. However, the paucity of research involving administration of higher doses and adopting more complex dosing protocols limits generalizability to real-life AmED consumption, and precludes conclusions regarding the dose-dependent effects of co-ingestion when consumers engage in excess intake of the two constituents.

1.3 Overall Objective and Research Questions

The overall aim of this thesis was to address the identified gaps in the field of research and provide an empirical evidence base regarding the potential harms of AmED use. The specific research questions which guided this doctoral research were as follows:

Question 1: Self-reported retrospective AmED consumption patterns

- What are the consumption patterns associated with AmED use at the community-level in regards to: (i) the frequency and quantity of intake, (ii) drink preferences, and (iii) consumption context?

Question 2: Self-reported retrospective AmED motivations

- What are the primary motivations driving AmED beverage choice at the community-level?

Question 3: Self-reported retrospective AmED consequences of use

- Based on the premise that AmED offers additional harms relative to alcohol, are there any appreciable differences in the physiological, psychological, and behavioural outcomes of AmED versus alcohol consumption when comparing retrospective self-reported drinking experiences for the same individual?

Question 4: Self-reported physiological and psychological outcomes of acute AmED dosing

- Following from *Question 3,* are any changes in self-reported physiological and psychological side-effects evident when comparing the effects of an acute dose of AmED and alcohol in a controlled environment for the same individual?

Question 5.1 and *5.2*: Objective risk-taking and impulsive behaviour outcomes of acute AmED dosing

- Following from *Question 3,* are any changes in objectively assessed risk-taking evident when comparing the effects of an acute dose of AmED and alcohol in a controlled environment for the same individual?
- Are any changes in objectively assessed impulsive behaviour (specifically impulsive response initiation, response disinhibition, and impulsive decision-making) evident when comparing the effects of an acute dose of AmED and alcohol in a controlled environment for the same individual?

Question 6.1 and *6.2*: Subjective and objective intoxication outcomes of acute AmED dosing

- Based on the premise that AmED reduces perceived intoxication, are any changes in objective intoxication (BrAC) and subjective intoxication (ratings of perceived intoxication) evident when comparing the effects of alcohol

alone and in combination with a high acute dose of ED (i.e., two or more standard 250mL EDs) in a controlled environment for the same individual?

- Following from *Question 6.1*, do objective and subjective intoxication outcomes differ dose-dependently according to the volume of ED co-administered with alcohol?

1.4 Design of Project

Three studies were undertaken with the aim of answering these research questions:

- *Study 1*: In order to address *Questions 1, 2* and *3*, an online self-administered survey of a convenience-sample of Australian community-based AmED consumers was undertaken[1]. Participants retrospectively self-reported their consumption patterns and motivations for AmED use, as well as the physiological, psychological, and behavioural consequences of AmED and alcohol use in the preceding six months. This study specifically focused on comparing the outcomes of AmED versus alcohol use for the same individuals (within-subject design). As noted in Section 1.2, this technique circumvents the confounding influence of systematic individual differences between consumer types.
- *Study 2*: In order to address *Questions 4*, *5.1* and *5.2*, a crossover, single-blind, placebo-controlled experimental study was undertaken to determine the effect of an acute alcohol dose consumed alone, and in combination with a low ED dose, on subjective physiological and psychological outcomes and

[1] Human Research Ethics Committee (Tasmania) Network approval reference number: H11734

objective measures of risk-taking and impulsive behaviour[2]. This study allowed for direct assessment of the pharmacological effects of AmED at a set dose, as the laboratory-based environment and blinding to treatment administration controlled for potential confounding variables (Section 1.3).

- *Study 3*: In order to address *Question 6.1* and *6.2*, a mixed design, single-blind, placebo-controlled experimental study was undertaken, where participants consumed each ED dose (0mL (placebo), 250mL, 500mL, and 750mL) in combination with one of three alcohol treatments: placebo, moderate (target BrAC .050%), or a high (target BrAC .080%) alcohol dose[3]. This study was undertaken to assess the pharmacological dose-dependent effects of AmED relative to alcohol on objective and subjective measures of intoxication in a controlled environment.

1.5 Organisation and Publications

The chapter structure of this thesis is outlined in Table 1, with specific reference to the research question (Section 1.5), study (Section 1.6), and publication comprising each chapter.

Chapter 2 provides a review of the literature by: outlining the independent effects of the two constituents; introducing the practice of co-ingesting; critiquing the current evidence base regarding the consumption patterns and motivations for AmED use; and describing the theorised oppositional pharmacological effects of alcohol and ED. The existing body of research assessing the effects of AmED is then systematically

[2] Human Research Ethics Committee (Tasmania) Network approval reference number: H12010
[3] Human Research Ethics Committee (Tasmania) Network approval reference number: H12010 (amended)

reviewed in a discrete publication, with a specific focus on AmED-related: (i) physiological, psychological, cognitive, and psychomotor outcomes, (ii) hazardous drinking practices, and (iii) risk-taking behaviour. It should be noted that this publication which outlines the primary gaps in the literature to provide a rationale for the current doctoral research was undertaken post-publication of those manuscripts comprising *Chapters 3*, *4*, and *6*.

The following two chapters outline the results of the descriptive study (*Study 1*). *Chapter 3* focuses on the reported antecedents and typical characteristics of AmED use, overviewing the AmED consumption patterns and motivations reported by the community-based convenience sample of Australian AmED consumers (*Question 1 and 2*). This sample also reported on the physiological, psychological, and behavioural consequences of AmED versus alcohol use in the preceding six months, the outcomes of which are outlined in *Chapter 4* (*Question 3*).

The remaining research chapters outline the results of the experimental studies directly assessing the pharmacological effects of AmED versus alcohol. *Chapter 5* relates the results of the crossover, placebo-controlled, single-blind experimental study comparing the self-reported physiological and psychological outcomes of acute AmED and alcohol dosing in a laboratory-based setting (*Study 2; Question 4*). Objective measures of behavioural outcomes, specifically risk-taking and behavioural impulsivity (impulsive response initiation, response disinhibition, and impulsive decision-making) were also administered in this study; the results of these analyses are reported in *Chapters 6* and *7* respectively (*Question 5.1 and 5.2*). *Chapter 8* outlines the results of the final experimental study, comparing the

objective and subjective intoxication outcomes of AmED and alcohol acute dosing in a laboratory-based setting to determine whether AmED alters intoxication and, if so, whether these changes were dose-dependent (*Study 3*; *Question 6.1 and 6.2*).

The final chapter, *Chapter 8*, comprises a general discussion and integration of these studies' results to determine if there is a coherent profile of additional alcohol-related harms with AmED consumption when examining: (i) consumption patterns and motivations for use, (ii) physiological and psychological outcomes of use, (iii) behavioural consequences of use, and (iv) objective and subjective intoxication state.

T**able 1**

Thesis Chapter Structure According to the Research Question and Study

Research Question	**Study**	**Thesis Chapter**	**Publication**
Literature Review (including systematic review)	-	2	*Addiction* (under review; commissioned): "'High' risk? A systematic review of the acute outcomes of mixing alcohol with energy drinks"
1. What are the consumption patterns associated with AmED use at the community-level in regards to: (i) the frequency and quantity of intake, (ii) drink preferences, and (iii) consumption context?	1	3	*Psychology of Addictive Behaviors* (2013): "Patterns of use and motivations for consuming alcohol mixed with energy drinks"
2. What are the primary motivations driving AmED beverage choice at the community level?	1	3	
3. Are there any appreciable differences in the physiological, psychological, and behavioural outcomes of AmED versus alcohol consumption when comparing retrospective self-reported drinking experiences for the same individual?	1	4	*Alcoholism: Clinical and Experimental Research* (2012): "The subjective physiological, psychological, and behavioral risk-taking consequences of alcohol and energy drink co-ingestion"
4. Are any changes in self-reported physiological and psychological side-effects evident when comparing the effects of an acute dose of AmED and alcohol in a controlled environment for the same individual?	2	5	*Appetite* (under review): "Self-reported physiological and psychological side-effects of an acute alcohol and energy drink dose"

Table 1 Continued

Research Question	Study	Thesis Chapter	Publication
5.1. Are any changes in objectively assessed risk-taking evident when comparing the effects of an acute dose of AmED and alcohol in a controlled environment for the same individual?	2	6	*Alcoholism: Clinical and Experimental Research* (2013): "The impact of alcohol and energy drink consumption on intoxication and risk-taking behavior"
5.2. Are any changes in objectively assessed impulsive behaviour (specifically impulsive response initiation, response disinhibition, and impulsive decision-making) evident when comparing the effects of an acute dose of AmED and alcohol in a controlled environment for the same individual?	2	7	*Journal of Psychopharmacology* (under review): "Laboratory behavioural assessment: The effect of an acute alcohol and energy drink dose on impulsivity"
6.1. Are any changes in objective intoxication (i.e., BrAC) and subjective intoxication (i.e., ratings of perceived intoxication) evident when comparing the effects of alcohol alone and in combination with a high acute dose of ED (i.e., two or more standard 250mL EDs) in a controlled environment for the same individual?	3	8	*Addiction* (under embargo): "'High' intoxication: The effects of alcohol and energy drink co-ingestion on breath alcohol concentration and perceived intoxication"
6.2. Do objective and subjective intoxication outcomes differ dose-dependently according to the volume of ED co-administered with alcohol?	3	8	
General Discussion	-	9	

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Chapter 2: Literature Review

2.1 Alcohol

2.1.1 Prevalence

Alcohol is one of the most popular psychoactive drugs consumed worldwide. In 2005, 40.6% of the world's population were current drinkers, consuming at least one standard drink within the past year, with an additional 13.6% identifying as former drinkers (Shield et al., 2013). Mean alcohol consumption per adult per capita globally in 2005 was 6.1 litres ethyl alcohol, with 40.6% of the population recorded as current drinkers (Shield et al., 2013). Comparatively, geographical analyses indicate higher intake amongst the Australian population, with mean alcohol consumption reaching 10.0 litres ethyl alcohol per adult.

2.1.2 Pharmacokinetics and Pharmacodynamics

Alcohol is rapidly and completely absorbed from the stomach and upper intestine, with maximum blood alcohol concentration (BAC) occurring within 30 to 90 minutes depending on the rate of gastric emptying (Julien, Advokat, & Comaty, 2011). Alcohol is metabolised primarily in the liver (85%) and the stomach (15%) in a series of stages, where: (i) the enzyme alcohol dehydrogenase and a co-factor (nicotinamide adenine dinucleotide; NAD) convert alcohol to acetaldehyde, (ii) acetaldehyde is converted by the enzyme aldehyde dehydroenase to acetic acid, and then (iii) acetic acid is broken down into carbon dioxide and water. BAC increases if alcohol consumption exceeds the rate of metabolism (Julien et al., 2011). First-pass gastric metabolism of alcohol reduces blood alcohol levels (BAL) by 15%. Knowledge of kinetics allows estimation of intoxication levels prior to drinking commencement, and rates of elimination after drinking cessation. However, metabolism and elimination is subject to intra-individual (e.g., time of day, beverage

type, food intake and composition) and inter-individual (e.g., genotype, sex, prior drinking experience, age, and weight) variation (Eckardt et al., 1998).

In regards to distribution, alcohol easily crosses the blood brain barrier, interrupting normal functioning of specific neurotransmitters, primarily the major excitatory and inhibitory systems. Alcohol has a depressant action on neural functioning, decreasing excitation and increasing inhibition. Specifically, acute alcohol consumption inhibits functioning of excitatory glutamatergic neurotransmission by depressing the responsiveness of ion-channel glutamate receptors, particularly N-methyl-D-aspartate (NMDA) receptors, and reduces NMDA-induced release of other neurotransmitters, such as dopamine, norepinephrine, and acetylcholine (Julien et al., 2011; Mukherjee, Das, Vaidyanathan, & Vasudevan, 2008). Disruption of NDMA receptor functioning, particularly following compensatory up-regulation of NMDA receptors after chronic consumption, has been linked with alcohol-induced learning and memory difficulties. In regards to the inhibitory system, acute alcohol consumption increases gamma-aminobutyric acid (GABA) transmission by increasing chloride ion flow, decreasing the activity of the neuron and resulting in behavioural change, including decreased attention, increased sedation and muscle relaxation, and changes in cognitive and motor skills (Julien et al., 2011; Mukherjee et al., 2008). Alcohol consumption is also thought to (directly and indirectly) impact on monoaminergic systems, with the positive reinforcing effects of alcohol attributed to changes in the dopaminergic, noradrenergic, and serotonergic systems, as well as endogenous opioid and GABAergic systems (Julien et al., 2011).

While alcohol is typically characterised by its depressant actions, there is evidence to suggest that alcohol can produce stimulatory effects, typically evident at lower BrAC and during the ascending limb of the blood alcohol concentration curve. Sedation effects are generally experienced at higher BrAC and during the descending limb of the blood alcohol concentration curve (Earleywine & Erblich, 1996). Thus, in most drinking circumstances, alcohol has a biphasic physiological and psychological effect, with stimulatory outcomes during alcohol absorption preceding sedation effects (Pohorecky, 1977). The typical profile of alcohol intoxication reflects the depressant neurological actions. While the effects of alcohol are dependent on pharmacological (e.g., dose), individual (e.g., tolerance, familial history of alcoholism) and environmental (e.g., peer influence) factors, acute alcohol consumption typically causes impairment across a range of cognitive and psychomotor processes, including divided attention, selective/focused attention, reaction time, behavioural inhibition, working memory, and visuo-motor control, particularly when ingested at higher doses (BrAC $\geq$ .070%) (Zoethout, Delgado, Ippel, Dahan, & van Gerven, 2011). Participants also typically display impaired motor performance, with poorer postural stability and oculomotor coordination (Zoethout et al., 2011).

2.1.3 Related Harms

Alcohol consumption can offer some protective health effects, including reduced likelihood of heart failure and stroke, as well as a decreased risk of diabetes and metabolic syndrome associated with obesity (Gunzerath, Faden, Zakhari, & Warren, 2004). However, these effects are only evident when alcohol is consumed regularly in low amounts, and are substantially outweighed by the negative consequences of

use when consumed in excess. Alcohol is responsible for considerable physical and psychological health harms, being one of the five leading risk factors contributing to the global disease burden in 2010 (Lim et al., 2012). In 2004, 3.8% of global deaths were ascribed to alcohol use (6.2% male and 1.1% female), with 42% of these cases attributed to acute intoxication (World Health Organisation, 2004). The most common causes of acute intoxication-related mortality were road traffic injuries (12%), other unintentional injuries (10%), violence (8%), self-inflicted injuries (4%), poisoning (3%), drowning (3%), and falls (2%).

The harms of acute alcohol intoxication are not restricted to the consumer. Nearly one-tenth (8%) of adult Australians reported in the 2010 National Drug Strategy Household Survey (Australian Institute of Health and Welfare, 2011) that they had been a victim of alcohol-related physical abuse, and a total of 277 deaths in 2005 were estimated to be due to another's drinking and driving. The economic burden of alcohol use extends across all aspects of society, resulting in reduced workplace productivity, increased burden on the healthcare and criminal justice systems, family problems, and public disorder (Manning et al., 2013). Estimates of societal economic costs in middle and high income countries typically exceed 1% of the gross national product, with population-weighted costs ranging between $358 and $837 per head in high income countries (Rehm et al., 2009). Looking at Australia specifically, the estimated societal economic cost of alcohol use for 2010 was $14,352 billion (20.6% criminal justice system, 11.7% health system, 42.1% Australian productivity, and 25.5% traffic incidents)[4] (Manning et al., 2013).

[4] This figure represents an underestimation of costs, as data were drawn from objective sources; indirect self-reported costs were not included (Manning et al., 2013).

Two primary factors are thought to contribute to the global disease burden and social economic costs of alcohol use: average intake and patterns of drinking, in particular, high risk drinking (Rehm et al., 2010; Rehm et al., 2003). High-risk drinking is typically defined according to recommended maximum intake guidelines to minimise injury or adverse health outcomes, but can also include drinking limits set for certain contexts (e.g., BAC limits for drink-driving). In Australia, consumption of no more than two standard drinks (10g alcohol per standard drink) per occasion is advised for healthy adults (18 years or older) to minimise lifetime risk of harm from alcohol-related disease or injury (National Health and Medical Research Council, 2009). In regards to acute high-risk drinking, the National Health and Medical Research Council (2009) advise consumption of no more than four standard drinks on a single occasion to minimise the risk of within-session alcohol-related injury. This recommendation is based on evidence suggesting that the relative risk of injury is more than twofold after consuming four drinks, with the risk increasing dramatically with higher intake.

In considering this latter guideline, a partial explanation can be offered regarding the sizeable economic and social burden of alcohol use in Australia, with elevated rates of high risk drinking amongst the population. Data from the 2010 National Drug Strategy Household Survey (Australian Institute of Health and Welfare, 2011) indicated that 40% of adult Australians reported a recent drinking episode that put them at risk of an alcohol-related injury, with 15% consuming alcohol at these levels on a weekly basis. This pattern of consumption was particularly prevalent amongst adolescents and young adults, with 32% of Australians aged between 18-19 years and 27% of those aged between 20-29 years reporting high-risk alcohol consumption.

2.1.4 Risk-Taking

2.1.4.1 Survey and Experimental Research

There is a strong body of epidemiological research showing an association between high-risk alcohol consumption and increased risk-taking, including driving behaviours (e.g., Quinlan et al., 2005), sexual behaviours (e.g., Fergusson & Lynskey, 1996), gambling (e.g., Barnes, Welte, Hoffman, & Dintcheff, 2002; Desai, Maciejewski, Pantalon, & Potenza, 2006), licit and illicit drug use (e.g., Degenhardt, Hall, & Lynskey, 2001; M. B. Reed, Wang, Shillington, Clapp, & Lange, 2007), and aggressive and antisocial behaviours (e.g., Komro et al., 1999), as well as physical injury and mental injury or harm (e.g., Caldwell et al., 2002; Cherpitel, 1993). These studies are important as they indicate that alcohol consumers are a group at increased risk of adverse outcomes. However, causal inferences regarding the pharmacological effects of alcohol on risk-taking behaviour cannot be drawn based on this research due to the potential confounding environmental (e.g., peer influence), individual (e.g., personality, attitudes) and pharmacological (e.g., alcohol tolerance) factors. For example, research has shown that the relationship between alcohol use and alcohol-related violence is modified by alcohol-aggression expectancies; specifically, high levels of alcohol consumption primarily predict alcohol-related aggression for individuals who believe that alcohol causes aggression (Barnwell & Earleywine, 2006).

Another limitation of these studies is that the majority rely on retrospective self-report. These methodologies introduce bias as they may depend upon accurate recall of events occurring within an extended timeframe, and accurate reporting of sensitive and potentially illegal behaviours. While laboratory-based research may

reduce ecological validity, assessing the effect of acute dosing in a controlled environment allows for direct measurement of the pharmacological effects of alcohol. Furthermore, systematic individual differences can be controlled by assessing behaviour by the same person after placebo and active alcohol administration (within-subject design). In contrast with the survey and epidemiological research, the experimental literature is somewhat mixed in regards to the direct effects of alcohol on risk-taking, particularly in regards to driving and financial risk-taking behaviour (Lane, Cherek, Pietras, & Tcheremissine, 2004). The following sections will review the research in this field in regards to these behaviours.

2.1.4.2 Experimental Research: Driving Risk-Taking

There is a strong body of epidemiological research supporting the association between alcohol use and motor vehicle accidents. An analysis of single vehicle driver fatalities showed that at 0.05% to 0.10% BAC the risk of a motor vehicle accident was nine times greater than at 0.00% BAC; at ≥0.15% BAC the risk of crashing was 300 to 600 times that when at 0.00% BAC (Zador, 1991). In further support, alcohol was the most commonly detected drug in analysis of blood samples from 2500 injured Australian drivers, with 8.6% (*n*=275) testing positive for alcohol, and 3.8% (*n*=34) testing positive for alcohol in combination with cannabinoids, benzodiazepines, and/or stimulants; 84.5% (*n*=261) of these drivers recorded an BAC in excess of the Australian legal driving limit of 0.05% (Longo, Hunter, Lokan, White, & White, 2000).

Despite this well-established association in epidemiological research, the experimental literature clarifying the pharmacological effect of alcohol on driving risk-taking is less clear-cut. Experimental research assessing driving behaviour has the advantage of increased ecological validity with the advent of driving simulators. As evident in Table 1, the majority of these studies show no statistically significant effect of alcohol on measures of driving risk-taking behaviour; increases in risk-taking typically only occurred in the context of experimenter manipulation of psychological state. For example, Oei and Kerschbaumer (1990) found that participants who consumed a moderate (mean BrAC at testing .040%) or high (mean BrAC at testing .080%) alcohol dose and received pro-drink driving information from a confederate peer drove faster compared to baseline, while participants who received anti-drink driving information did not alter their driving speed[5]. Similarly, Burian, Hensberry, and Liguori (2003) found that when participants received (mean peak BrAC .048%) but did not expect alcohol, the probability of a risky lane choice tended to significantly increase compared to when they did not expect or receive alcohol. However, this effect was reversed when participants received the same dose of alcohol and also expected the beverage, with participants showing a statistically significant decrease in the probability of a risky lane choice. These results suggest that, regardless of the pharmacological effects of alcohol, consumers' preconceptions and beliefs regarding the effects of alcohol may influence their subsequent behaviour.

[5] It should be noted that the authors drew these conclusions based on interpretation of the descriptive data following identification of a statistically significant interaction between alcohol dose (baseline, .040% BrAC, and .080% BrAC) and drink-driving attitude (anti or pro-drink driving condition); paired comparisons of the conditions in follow-up analyses were not undertaken.

Another factor to consider in these studies is the consequences of the risk-taking behaviour. Risk-taking behaviour is defined as the selection of a response which has an unknown probability of providing a reinforcing or aversive outcome (Lane et al., 2004); the individual must weigh up the likelihood of the consequence, as the outcome will be dependent on their decision. The majority of studies outlined in Table 1 involved risk-taking assessment in an environment where the consequences were hypothetical or lacked personal significance. However, direct tangible rewards and penalties contingent on the individual's behaviour have been shown to influence risk-taking behaviour. For example, Fillmore, Blackburn, and Harrison (2008) found that increases in risky driving behaviour, indexed by failures to stop at red lights, after a high alcohol dose (mean peak BrAC .089%) were exacerbated when participants were placed under response conflict, whereby participants were offered monetary reimbursement for quickly completing the drive while also safely stopping at red traffic lights.

This body of literature emphasises the need for consideration of the context in which behaviour is enacted when conducting research in controlled settings. Strategies to maximise ecological validity (e.g., individual consequences for behaviour) may be necessary to provide an accurate picture of the effects of alcohol on risk-taking. This is particularly important when controlling for external situational factors (e.g., expectancy effects) which could co-contribute to behavioural outcomes.

Table 1

Effect of Alcohol Administration on Driving Risk-Taking in Experimental Research

Author	*N*[a]	Design[b]	Blinding[c]	Placebo/ Control	Task	Risk-Taking Indicator	Task-Dependent Reimbursement	Alcohol Dose[d]	Alcohol BrAC (%)[e]	Outcome[f]
Burian, Liguori, and Robinson (2002)	13 (13)	Within-subject	ns (single blind)	Placebo	Driving simulator	Frequency of selecting narrow lane according to penalty	Participant with highest points receives a monetary prize	0.3g/kg	~.029	=
								0.5g/kg	~.056	↑^
								0.8g/kg	~.095	=
Burian et al. (2003)	58 (30)	Between-subject	Double-blind#	Placebo	Driving simulator	Frequency of selecting narrow lane according to alcohol expectancy	Participant with highest points receives a monetary prize	0.5g/kg	.048	↑^ and ↓^
Cohen, Dearnaley, and Hansel (1958)	ns	Between-subject	None	Control	Manual vehicle	Width of narrowest gap traversed	No	56.8ml	.004	=
								170.4ml	.058	↑
Fillmore et al. (2008)	14 (7)	Within-subject	ns (single blind)	Placebo	Driving simulator	Number of traffic light stopping failures	Reward-penalty structure based on time and compliance with road rules (response conflict condition)	0.65g/kg	.089	↑^
						Acceleration from traffic light stops				↑^
						Driving speed				↑^
Kearney and Guppy (1988)	24 (24)	Within-subject	ns (single blind)	Placebo	Manual vehicle	Speed estimation	No	100mg/ dL	.095	=
Leung and Starmer (2005)	32 (18)	Within-subject	ns (single blind)	Placebo	Driving simulator	Headway distance between own vehicle and vehicle being overtaken	Monetary bonus for clear experimental driving record	0.7g/kg	.064	=
						Overtaking speed				=

Table 1 Continued

Author	*N*[a]	Design[b]	Blinding[c]	Placebo/ Control	Task	Risk-Taking Indicator	Task-Dependent Reimbursement	Alcohol Dose[d]	Alcohol BrAC (%)[e]	Outcome[f]
McMillen and Wells-Parker (1987)	39 (ns)	Between-subject	Double-blind#	Control Placebo	Video driving game simulator	Frequency of passing cars	No	13mL/18kg	ns	=
								45mL/18kg	ns	=
						Time at high speed		13mL/18kg	ns	=
								45mL/18kg	ns	=
McMillen, Smith, and Wells-Parker (1989)	96 (64)	Between-subject	Double-blind	Placebo	Video driving game	Frequency of passing cars	No	22mL/18kg	.070	=
						Frequency of lane changes				=
						Time at maximum speed				=
Oei and Kerschbaumer (1990)	36 (18)	Between-subject	ns	Baseline	Video driving game simulator	Mean maximum speed (according to peer-induced drink driving attitude)	No	1mL/kg (multi-dose)	.040	=^ and ↑^
									.080	=^ and ↑^
R. West, Wilding, French, Kemp, and Irving (1993)	15 (6)	Within-subject	Double-blind	Placebo	Video visual display whilst sitting in car	Driving speed	No	.025%	.024	=
								.050%	.052	=

Note. [a] The number in brackets represents the number of male participants. [b] The design is specified based on the alcohol dosing protocol (between or within subjects). [c] Single-blind indicates that participants were blind to treatment condition, double-blind indicates that participants and data collectors were blind to treatment condition, and 'ns' means that blinding was not specified, although in some cases participant-blinding can be tentatively inferred from use of a placebo condition; note that # indicates that the study assessed the effects of alcohol expectancy, and thus some participants were accurately informed of their beverage content. [d] The alcohol dose was either given as a set dose or calculated according to participant body weight (g/kg or mL/kg), a target breath alcohol concentration (% BrAC) or blood alcohol level (mg/dL BAL). [e] The BrAC reported reflects the peak mean BrAC recorded for the study (overall or within a condition); note that figures indicated with ~ are estimates derived from graphical depictions of BrAC and thus are approximate and to be treated with caution. [f] This column indicates whether alcohol administration significantly (p<.050) increased (↑), decreased (↓), or did not alter (=) driving risk-taking relative to placebo/control administration/baseline; ^ For the following studies a significant effect of alcohol relative to placebo/control/baseline was only recorded in specific conditions: Burian et al. (2002): significant alcohol-induced increase in risk-taking in the high penalty condition (where participants lost 5 points from 100 for each lane cone knocked over) and not in the lower penalty conditions (1 or 3 points subtracted); Burian et al. (2003): (i) trend (p=.080) towards a significant alcohol-induced increase in risk-taking when participants received but did not expect alcohol compared to when they did not expect or receive alcohol and (ii) a significant decrease in risk-taking when participants received and expected alcohol compared to when alcohol was not expected nor received; Fillmore et al. (2008): (i) significant alcohol-induced increase in traffic light stopping failures evident for the response conflict condition (monetary reinforcement for quick responses to go targets and low rates of commission errors) and not in the no response conflict condition (no monetary reinforcement for performance), (ii) significant alcohol-induced increase in the acceleration from traffic light stops and in drive speed, regardless of response conflict condition; Oei and Kerschbaumer (1990): significant alcohol-induced increase in risk-taking present in the pro drink-driving attitude condition (where participants received pro drink-driving information from a confederate) at both time points (.040% and .080%), with no major change in risk-taking after alcohol relative to baseline in the anti-drink-driving condition, although it should be noted that these conclusions are based on descriptive interpretation of a significant interaction, with no pairwise comparisons conducted.

2.1.4.3 Experimental Research: Financial Risk-Taking

Overall, the lack of consistent support for alcohol-induced increases in driving risk-taking suggests that psychological factors may interact with the pharmacological effects of alcohol to cause changes in behaviour. Despite epidemiological research showing an association between alcohol use and financial risk-taking (Welte, Barnes, Wieczorek, Tidwell, & Parker, 2001), the experimental literature regarding the effects of alcohol on gambling behaviour presents a similar picture as evident for driving behaviour (Table 2). Those studies which show alcohol-induced increases in risk-taking behaviour have generally incorporated clearly specified reward and penalty contingencies into procedures (e.g., Gilman, Smith, Ramchandani, Momenan, & Hommer, 2012). However, inclusion of reinforcement schedules does not guarantee alcohol-induced increased risk-taking; several studies have revealed equivalent behavioural outcomes in active and placebo alcohol conditions despite introducing task-dependent monetary reimbursement (e.g., Breslin & Sobell, 1999).

These equivocal outcomes are further complicated, in that several studies showing equivalent overall rates of risk-taking behaviour have demonstrated alcohol-related changes in gambling strategy throughout the task after analysing performance at different time points. For example, Euser, van Meel, Snelleman, and Franken (2011) found that alcohol consumption (mean peak BrAC .077%) did not impact overall performance on the Balloon Analogue Risk-Task (BART; Lejuez et al., 2002). The BART is a computerised laboratory-based measure of sequential risk-taking task where participants inflate simulated balloons (higher pumps equals greater risk-taking). This task has the advantage of simulating real-life risk-taking, as participants experience monetary consequences of decision-making during the task, with risk-

taking behaviour rewarded up until a point at which further risk-taking results in poorer outcomes (Lejuez et al., 2002). Decomposition of the task (*N*=60 trials) into three blocks showed that the alcohol group significantly decreased their number of pumps from Block 1 (initial 20 trials) to Block 2 and Block 3 (final 20 trials). In contrast, the placebo group started off cautiously and increased the number of risky choices throughout the task, nearing the optimal balance of pumps in Block 3. Thus, while both groups ended up with a similar overall outcome, the alcohol group shifted from a riskier to a more cautious strategy, failing to reach the optimal balance of pumps. These outcomes could explain the discrepant findings in past research, as analyses based on overall outcomes may obscure changes in gambling strategy throughout the task.

2.1.5 Alcohol: Summary

Alcohol is one of the most popular substances consumed worldwide, with two-fifths of the global population reporting current use. Alcohol interrupts normal functioning of specific neurotransmitters, acting primarily as a depressant by increasing inhibition and decreasing excitation. While alcohol can exert some stimulant effects at low BrAC and during the ascending limb of the blood alcohol concentration curve, the characteristic depressant effects of alcohol include impaired cognitive and behavioural performance and increased sedation-related physiological and psychological side-effects. Acute alcohol intoxication following excess intake causes a considerable social and economic burden in regards to the harms experienced by the consumer and those around them.

Table 2

Effect of Alcohol Administration on Gambling Risk-Taking in Experimental Research

Study	*N*[a]	Design[b]	Blinding[c]	Placebo/ Control	Task	Risk-Taking Indicator[d]	Task-Dependent Reimbursement	Alcohol Dose[e]	Alcohol BrAC (%)[f]	Outcome[g]
Balodis, MacDonald, and Olmstead (2006) *Sample 1*	127 (127)	Between -subject	ns (single-blind)	Control Placebo	Computerised Iowa Gambling Task with varying reward magnitude and penalty magnitude/probability	Net score	No	.080%	.093	=
Balodis et al. (2006) *Sample 2 (participant knowledge of experiment purpose)*	50 (31)	Between -subject	None	Control Placebo	Computerised Iowa Gambling Task with varying reward magnitude and penalty magnitude/probability	Net score	No	.080%	.093	=
Breslin and Sobell (1999)	108 (53)	Between -subject	None	Control Placebo	Computerised binary choice task with varying probability and magnitude of wins and losses	Mean rank of risk	Option for bonus payment based on betting performance with high/low probability and pay-off	.080%	.079	=
Cronce and Corbin (2010)	130 (70)*	Between -subject	Double-blind	Placebo	Simulated slot machine with three gambling outcome conditions (win, breakeven, loss).	Gambling persistence Average bet per trial	Informed could choose to receive bonus up front or contingent on betting performance	0.84g/kg	.073	=/↑^ ↑^
Euser et al. (2011)	64 (64)	Between -subject	None	Placebo	Balloon Analogue Risk Task	Average number of pumps	Participant with highest points receives a prize	0.65g/kg	.077	=

Table 2 Continued

Study	*N*[a]	Design[b]	Blinding[c]	Placebo/ Control	Task	Risk-Taking Indicator[d]	Task-Dependent Reimbursement	Alcohol Dose[e]	Alcohol BrAC (%)[f]	Outcome[g]
George, Rogers, and Duka (2005)	32 (16)	Between-subject	Double-blind	Placebo	Computerised binary outcomes gambling task with varying probability of winning and magnitude of reward/loss	Proportionate choice losses only trials gains	Participant with highest points receives a prize	0.60g/kg	.076	↑^
Gilman et al. (2012)	20 (8)	Within-subject	Double-blind	Placebo	Computerised discrete trial binary choice (risky versus safe) gambling task with differing probability and magnitude of gain/loss	Percentage of risky choices	Reward dependent on task performance with different probabilities	.080%	.070	↑
Kyngdon and Dickerson (1999)	40 (40)	Between-subject	ns	Placebo	Analogue game	Persistence at gambling while losing	Reward dependent on task performance with different probabilities	31g	ns	↑
Lane et al. (2004)	16 (8)	Within-subject	ns (single blind)	Placebo	Computerised discrete trial binary choice gambling differing probability and magnitude of gain/loss	Assessing preference for risky and non-risky choice	Bonus contingent on betting performance	0.2g/kg 0.4g/kg 0.8g/kg	~.017 ~.043 ~.085	= ↑ ↑
Meier, Brigham, Ward, Myers, and Warren (1996) *Study 1*	10 (10)	Within-subject	ns (single-blind)	Placebo	Computerised binary outcomes gambling task with differing certainty and severity of outcomes	Willingness to gamble	Participant with highest points receives a prize	.010-.049% .050-.099% .100-.150%	.030 .076 .130	= = =

Table 2 Continued

Study	*N*[a]	Design[b]	Blinding[c]	Placebo/ Control	Task	Risk-Taking Indicator[d]	Task-Dependent Reimbursement	Alcohol Dose[e]	Alcohol BrAC (%)[f]	Outcome[g]
Meier et al. (1996) *Study 2*	10 (10)	Within-subject	ns (single-blind)	Control	Computerised binary outcomes gambling task with differing certainty and severity of outcomes	Willingness to gamble	Participant with highest points receives a prize	.100-.150%	.110	=
Meier et al. (1996) *Study 3*	84 (84)	Between-subject	None	Control	Binary outcomes gambling task in a bar setting	Willingness to gamble	Participant with highest points receives a prize	.010-.049% .050-.090% ≥.100%	.010-.049 .050-.090 .100-.117	= = =
Phillips and Ogeil (2007)	20 (20)	Within-subject	None	Baseline	Computerised Blackjack game with high/low stakes and presence of decision aid (Basic advice)	Proportion of failure to stand errors	No	.070%	.048	↑^
S. C. Reed, Levin, and Evans (2012)	46 (0)	Within-subject	Double-blind	Placebo	Balloon Analogue Risk Task	Adjusted average number of pumps	Yes	0.5g/kg 0.75g/kg	.056 .092	= =
Reynolds, Richards, and de Wit (2006b)	24 (11)	Within-subject	Double-blind	Placebo	Balloon Analogue Risk Task	Adjusted average number of pumps	Yes	0.4g/kg 0.8g/kg	~.037 ~.076	=

Note. [a] The number in brackets represents the number of male participants; * indicates that this number was calculated from information provided in the manuscript. [b] The design is specified based on the alcohol dosing protocol (between or within subject). [c] Single-blind indicates that participants were blind to treatment condition, double-blind indicates that participants and data collectors were blind to treatment condition, 'none' means that both participant and data colletor were aware of treatment administration, and 'ns' means that blinding was not specified, and 'ns' means that blinding was not specified, although in some cases participant-blinding can be tentatively inferred from use of a placebo condition. [d] Note that 'net score' was defined as the advantageous card decks draws minus disadvantageous card deck draws, 'mean rank of risk' was based on an index of choices according to level of risk, and 'persistence at gambling while losing' was calculated based on the number of gambling trials and amount wagered. [e] The alcohol dose was either consistent for each participant (set) or calculated according to participant bodyweight (g/kg) or according to a target breath alcohol concentration (% BrAC). [f] BrAC reported reflects the peak mean BrAC recorded for the study (overall or within a condition); note that figures indicated with ~ were estimates derived from graphical depictions of BrAC and thus should be treated with caution; # indicates that blood alcohol concentration (BAL) was assessed. [g] This column indicates whether alcohol administration significantly ($p<.050$) increased (↑), decreased (↓), or did not alter (=) driving risk-taking relative to placebo/control administration; ^ For the following studies a significant effect of alcohol relative to placebo/control was only recorded in specific conditions: Cronce and Corbin (2010): (i) overall analysis of gambling persistence did not show a significant effect of alcohol, however breakdown analyses showed that participants in the alcohol condition who persisted in gambling until they had zero credit lost their available funds in significantly fewer trials compared to individuals in the placebo condition, and (ii) average bet per trial was significantly higher after alcohol relative to placebo for low trait impulsivity participants, with no significant change for high trait impulsivity participants; George et al. (2005): when the losses were large and the probability of winning high, participants in the placebo condition could discriminate between different magnitudes of gain; in contrast, participants in the alcohol did not show this level of discrimination; Phillips and Ogeil (2007): significant alcohol-induced increase in risk-taking relative to baseline performance evident only when a decision aid was present (participant informed 'advised to hit' or 'advised to stand').

Survey and epidemiological research consistently points towards a strong association between alcohol consumption and increased engagement in risk-taking behaviours, suggesting that alcohol consumers are at an elevated risk of harm. Assessing the effects of acute alcohol administration on risk-taking behaviour in laboratory-based settings can clarify the direct pharmacological effects of alcohol intoxication, as the controlled environment and blinding of active and placebo treatments minimises the impact of potential confounding variables which could influence behaviour during real-life drinking sessions. Examination of this body of research, particularly in regards to driving and financial risk-taking, indicates that alcohol-induced increases in risk-taking may occur when participant expectancies or attitudes towards the behaviour are manipulated, or when tangible consequences are enforced during the intoxication experience. The latter methodological consideration is important from an ecological validity perspective, as real-world risk-taking behaviour incurs consequences which are tangible and personal to the individual. Consistent implementation of task-dependent reward and penalty contingencies into assessment procedures may increase task sensitivity and maximise generalisability to real-world alcohol-related risk-taking behaviour.

2.2 Energy Drinks

2.2.1 Prevalence

EDs are stimulant beverages promoted as facilitating performance by reversing fatigue effects and increasing alertness (Heckman et al., 2010). Unlike alcohol, EDs are a relatively new psychoactive substance. Despite originating over half a century ago in Asia and Europe, EDs only attained popularity following formation of the Red Bull® brand in Austria and introduction to United States consumers in 1987 and 1997, respectively (Reissig, Strain, & Griffiths, 2009). Since then, ED use has increased exponentially, with Australian data indicating that ED sales swelled from 2.8 million litres in 1997 to 13.9 million litres in 2006 (Levy & Tapsell, 2007).

The few studies assessing prevalence of ED use have typically focused on university student or regional samples in the United States, Canada, and Europe (Table 3). These studies indicate that ED use is a normative practice among certain subgroups, particularly those who also display high-risk alcohol use behaviours, with 48% to 81% of surveyed university students reporting use of ED in their lifetime (Attila & Cakir, 2011; L. Berger et al., 2011; Marczinski, 2011; Miller & Quigley, 2011; Oteri, Salvo, Caputi, & Calapai, 2007). This high proportion of university students identifying as ED consumers is not surprising considering that the primary motivations for use typically revolve around the functional nature of the beverages (Attila & Cakir, 2011; Buxton & Hagan, 2012). For example, 67% of a United States university student sample used EDs to combat insufficient sleep, 65% to increase their energy, 50% while studying, 45% while driving for an extended duration, and 17% to reduce alcohol hangover effects (Malinauskas, Aeby, Overton, Carpenter-Aeby, & Barber-Heidal, 2007).

Table 3

Percentage of ED Users in Cross-Sectional Samples

Study	*N*[a]	Demographics[b]	ED Consumers(%)[c]
			Yesterday
Ludden and Wolfson (2010)	197 (96)	United States school students (age ns)	6
			Last week
Buxton and Hagan (2012)	180 (148)	Ghana university student athletes (47% 21-23 years, 27% 24-26 years)	62
Park, Onufrak, Blanck, and Sherry (2013)	25,492 (12,236*)	United States adult civilian nationally representative sample (13% 18-24 years, 26% 25-39 years, 36% 40-59 years, 24% 60≥ years)	31
Stasio, Curry, and Wagener (2011)	107 (60)	United States university student athletes (*n*=44), Reserve Officer Training Corp cadets (*n*=18), and undergraduate university students (*n*=45) (age ns)	57
Velazquez, Poulos, Latimer, and Pasch (2012)	585 (260*)	United States university students (*M*=18.7 years)	18
			Last month
Malinauskas et al. (2007)	496 (ns)	United States undergraduate university students (*M*=21.5, *SD*=3.7 years)	51^
Miller (2008b)	795 (413*)	United States undergraduate university students (*M*=20.0 years)	39
Miller (2008a)	602 (313*)	United States undergraduate university student s(*M*=20.0 years)	38
Norton, Lazev, and Sullivan (2011)	613 (421)	United States undergraduate psychology students who had consumed caffeine in past month (age ns)	42
Velazquez et al. (2012)	585 (260*)	United States university students (*M*=18.7 years)	38
Wells et al. (2013)	1469 (781)	United States nightlife venue and college bar patrons (*M*=26.4, *SD*=4.6 years)	34
D. S. West et al. (2006)	253 (90*)	United States undergraduate university students (age ns)	20
			Last 6 months
Sindich and Burns (2011)	693 (402*)	Australian regular ecstasy users (*M*=24.0, *SD*=6.1 years)	70
			Last 12 months
Arria et al. (2011)	1097 (505*)	United States fourth year university students (range 20-23 years)	66
Hoyte, Albert, and Heard (2013)	462 (276)	United States university student athletes (*M*=20.9 years)	80

Table 3 Continued

Study	*N*[a]	Demographics[b]	ED Consumers (%)[c]
			'Ever' used
Arria et al. (2010)	1060 (488*)	United States undergraduate university students (age ns)	~37
Attila and Cakir (2011)	439 (222)	Turkish medicine, sports, and arts university students (*M*=22.8, *SD*=2.1, range 19-39 years)	48
Ballistreri and Corradi-Webster (2008)	211 (114)	Argentine fourth year physical education university students (*M*=22.6, *SD*=2.25, range 21-38 years)	65
L. Berger et al. (2011)	946 (ns)	United States residents of Milwaukee, Wisconsin (range 18-92 years)	31
Marczinski (2011)	706 (354)	United States psychology university students (*M*=20.9 years)	81
Miller and Quigley (2011)	226 (136*)	United States musicians residing in New York (*M*=22.7, *SD*=8.22, range 18-45 years)	57
Nordt et al. (2012)	2,158 (1,038*)	United States patients attending two San Diego emergency departments (age ns)	60
Oteri et al. (2007)	450 (186*)	Italian medicine university students (*M*=24.5, range 19-30 years)	57

Note. [a] The figure in parentheses represents the number of male participants; ns indicates that the data was not specified and * indicates that the number was calculated from percentages provided in the manuscript and should be treated with caution. [b] This column details the sample characteristics, with information regarding age of participants indicated in brackets. [c] This column indicates the percentage of the sample who reported ED use within the time period specified; ^ indicates that the value represents the weighted percentage of lifetime ED users in the undergraduate cohort for that year level; ˜ indicates that the percentage refers to number of participants who reported drinking more than one ED per month in an average month.

2.2.2 Pharmacokinetics and Pharmacodynamics

ED ingredient composition and quantity can vary according to the country's governing regulatory body. However, the typical ED constituents contained in the primary EDs marketed in Australia include: (i) *caffeine* (1,3,7-trimethylxanthine), a natural plant product which functions as a central nervous system stimulant and increases arousal and vigilance (Parrot, Morinan, Moss, & Scholey, 2004), (ii) *taurine* (2-aminoethane sulfonic acid), a free amino acid widely distributed throughout the body which is implicated in several metabolic processes and argued to be a conditionally essential nutrient (Clauson, Shields, McQueen, & Persad, 2008; Finnegan, 2003; Huxtable, 1992), (iii) *glucose* and *sucrose*, major sources of fuel required for the normal functioning of the central nervous system (Clauson et al., 2008), (iv) *glucuronolactone*, a natural glucose metabolite (Food Standards Australia and New Zealand, 2001), and (v) *B vitamins*, a group of vitamins required for cellular processes, including energy production (Heckman et al., 2010; Higgins, Tuttle, & Higgins, 2010) (Table 4).

While the independent functions of these ED ingredients are generally well-understood, there is limited data regarding their interactive impact on performance. It has been theorised that some of the primary ED ingredients are present at sub-therapeutic doses (taurine), or included primarily to enhance the pleasurable taste of the beverage (glucose and sucrose) (Clauson et al., 2008). In contrast with the latter explanation, recent research indicates that an interaction of caffeine and glucose may contribute to the performance-enhancing effects of EDs, with greater facilitation of memory and attentional task performance following co-ingestion of caffeine (75mg caffeine) and glucose (37.5mg) relative to independent administration (Scholey &

Kennedy, 2004). Despite this, consensus amongst researchers at present identifies caffeine as the primary psychoactive ED ingredient (Reissig et al., 2009). Consequently, the majority of research has been focused on caffeine when drawing inferences regarding the fate of ED in the body and the biochemical and physiological outcomes of consumption.

Table 4

Ingredient Composition of Primary EDs Marketed in Australia (mg per 250mL)

Ingredient	**Red Bull®**	**Mother®**	**V®**	**Rockstar®**	**Monster®**
Taurine	1000	1000	500	1000	1000
Caffeine	80	80	77.5	80	80
Glucuronolactone	600	300	62.5	-	5
Inositol	50	30	50	25	5
Vitamin B2 (riboflavin)	-	-	1.23	3.5	1.8
Vitamin B3 (niacin)	20	4.5	7.25	20	20
Vitamin B5 (pantothetic acid)	5	1.75	1.75	-	-
Vitamin B6 (pyridoxine)	5	0.5	1.15	5	2.13
Vitamin B12 (cobalamin)	.005	.00025	.00143	.005	.005
Ginseng Root Extract	-	-	-	50	205
Guarana Seed Extract	-	-	300	25	5

Note. As ingredient composition information was derived from product packaging rather than chromatographic analysis, labelled and actual content may be subject to variation. Additionally, quantities may differ for EDs packaged as shots (i.e., 50-60mL), capsules, or powders; - denotes the absence of the ingredient in the particular product.

Similar to alcohol, orally ingested caffeine is rapidly and fully absorbed, generally reaching peak absorption between 30 and 45 minutes following consumption, with a plasma half-life of 5 to 6 hours (Marks & Kelly, 1973; A. Smith, 2002). Caffeine stimulates the central nervous system by acting as a non-selective adenosine receptor antagonist (see Fredholm, Battig, Holmen, Nehlig, & Zvartau, 1999 for a full review of the pharmacological actions of caffeine). Adenosine receptors modulate the release of central nervous system neurotransmitters, generally exerting sedative, depressant, and anticonvulsant actions (Kenemans & Lorist, 1995). Consequently, the neurochemical effect of caffeine as a competitive inhibitor results in the release of norepinephrine, dopamine, and serotonin, increasing arousal and alertness (Fisone, Borgkvist, & Usiello, 2004; Lorist & Tops, 2003).

Like alcohol, the effects of caffeine are dependent on pharmacological factors (e.g., dose; Attwood, Higgs, & Terry, 2007; Lorist & Tops, 2003; A. Smith, 2002), individual factors (e.g., state of withdrawal and fatigue; Lorist, Snel, & Kok, 1994a; Rogers et al., 2005), and situational factors (e.g., task difficulty; Peacock, Martin, & Carr, 2013d). However, consumption of a moderate caffeine dose (approximately 75mg to 400mg) typically improves attention (Lorist, Snel, Kok, & Mulder, 1994b; A. Smith, Maben, & Brockman, 1994), information processing (Haskell, Kennedy, Wesnes, & Scholey, 2005; Lorist et al., 1994a), working memory (Haskell et al., 2005), and vigilance (Brice & Smith, 2002; Childs & de Wit, 2006; Koelega, 1993). Furthermore, caffeine administration typically produces decreased ratings of fatigue, and increased ratings of wellbeing, happiness, energy, alertness, and sociability (Childs & de Wit, 2006; Haskell, Kennedy, Milne, Wesnes, & Scholey, 2008; Haskell et al., 2005; Yeomans, Ripley, Davies, Rusted, & Rogers, 2002). In regards

to the physiological effects, caffeine typically increases cardiac contractility and cardiac output[6] , enhances metabolic rate, escalates urine excretion, heightens respiratory rate and tidal volume (i.e., amount of air exhaled or inhaled), and alters muscle force contraction (Childs & de Wit, 2006; Griffiths, Juliano, & Chausmer, 2003; Julien et al., 2011; Nawrot et al., 2003). It is important to note that the positive effects of caffeine can dissipate with the consumption of large doses (≥ 400mg), evident via poorer performance, greater tension, and increased anxiety (Attwood et al., 2007; Lorist & Tops, 2003; A. Smith, 2002)

Examination of the experimental research assessing the effects of the whole beverage shows that the functional claims made in regards to ED are generally supported, particularly in regards to facilitated attention, vigilance, and psychomotor performance (Anderson, 2007; Childs & de Wit, 2008; Seidl, Peyrl, Nicham, & Hauser, 2000; Smit, Cotton, Hughes, & Rogers, 2004; Smit & Rogers, 2002) (Table 5). More ecologically valid laboratory-based measures of attention and motor performance also show performance-enhancing effects of ED consumption, with reduced lane weaving and steering deviation during driving simulator tasks following administration of one and two standard 250mL EDs (Mets et al., 2011a; Reyner & Horne, 2002) (Table 6). These positive functional effects also generally extend to the consumer's subjective state. The experimental literature shows that low-to-moderate ED dose administration (equivalent to one to two standard 250mL ED serves; 80mg to 160mg caffeine) typically results in lower ratings of fatigue, as well as increased ratings of alertness, stimulation, energetic arousal, hedonic tone, and overall mood, relative to control (Anderson, 2007) and placebo (Howard &

[6] It should be noted that decreased heart rate is generally only evident for consumers with low tolerance, with ameloriated of this effect for higher tolerance consumers.

Marczinski, 2010; Mets et al., 2011a; Smit et al., 2004) treatment conditions (Table 7).

2.2.3 Related Harms

While there is a strong evidence base supporting these positive psychological effects of ED, negative stimulant effects have also been described in the experimental literature, with participants reporting increased subjective 'jittery' and 'tense' ratings following ingestion of 250mL ED (80mg caffeine) relative to placebo (Smit et al., 2004). In regards to physiological outcomes, double-blind placebo-controlled studies have generally revealed mixed findings: (i) Alford, Cox, and Wescott (2001) and Ragsdale et al. (2010) reported equivalent cardiovascular functioning following ED consumption (one standard 250mL ED; 80mg caffeine) relative to placebo, (ii) Franks, Schmidt, McCain, and Fraer (2012) reported that regular ED dosing increased mean, systolic, and diastolic blood pressure over a 24-hour period relative to a caffeine (80mg) control beverage[7], whilst (iii) Gershon, Shinar, and Ronen (2009) reported that ED consumption (two standard 250mL EDs; 160mg caffeine) decreased heart rate variability during a driving simulator task relative to placebo. While the profile of cardiovascular harms post-ED consumption is inconsistent, the experimental literature indicates other potential adverse physiological outcomes of use. Relative to a control condition, consumption of two standard 250mL EDs (160mg caffeine) shortened daytime sleep time and reduced sleep efficiency following a simulated night-shift (Jay, Petrilli, Ferguson, Dawson, & Lamond,

[7] In the study by Franks et al. (2012), regular ED dosing involved administration of four standard 250mL EDs containing 80mg caffeine per standard beverage over an 11 hour period. When completing the caffeine control beverage condition, participants received four serves of bottle water containing 80mg of caffeine solution per serve

2006). Furthermore, consumption of three standard 250mL EDs (240mg caffeine) has been shown to increase urine output and urinary concentration of sodium relative to placebo administration (Riesenhuber, Boehm, Posch, & Aufricht, 2006).

This disturbance in the central nervous system is reflected in consumer reports of the side-effects occurring in natural drinking environments. One-third (29%) of self-identified ED users in a United States university student convenience sample (*n*=253) reported experiencing weekly jolt and crash episodes (a period of increased stimulation followed by a sharp, sudden drop in energy) and one-fifth experienced headaches and heart palpitations (22% and 19%, respectively) (Malinauskas et al., 2007). Over half (57%) of those who experienced jolt and crash episodes had ingested three or more EDs (i.e., at least 240mg caffeine) on one occasion. Similarly, 34% of ED users in a convenience sample of United States emergency department patients (*n*=1298) reported ever having an adverse reaction to ED use, the most common being jitteriness and/or shaking, palpitations and/or fast heartbeat, and difficulty sleeping (Nordt et al., 2012). Finally, a survey of retrospective self-reported sleep behaviour completed by a convenience sample of university student athletes (*N*=107) showed a significant weak to moderate positive correlation between frequency of ED use and disturbance of subjective sleep quality, sleep latency, sleep duration, and habitual sleep efficiency (Stasio et al., 2011).

Table 5

The Effect of ED Ingestion on Simple, Choice, and Recognition Reaction Time and Accuracy

Study	***N*[a]**	**Design[b]**	**Blinding[c]**	**Placebo/ Control**	**Task**	**Energy Drink Condition[d]**	**Simple RT[e]**	**Choice RT[e]**	**Recognition RT[e]**	**Accuracy[e]**
Alford et al. (2001) *Study 1*	10 (5)	Within-subject	Double blind	Control	5-choice reaction time task	~250ml	-	↓	-	-
Alford et al. (2001) *Study 2*	14 (7)	Within-subject	ns	Control	5-choice reaction time task	~250ml				
Gendle, Smucker, Stafstrom, Helterbran, and Glazer (2009)	36 (18)	Between-subject	Double blind	Placebo	Continuous performance task	~250ml	-	-	=	=
Gershon et al. (2009)	20 (13)	Within-subject	ns (single blind)	Placebo	Secondary visual choice reaction time task (primary task: driving simulator task)	~500mL	-	↓	-	-
Horne and Reyner (2001)	11 (6)	Within-subject	Double blind	Control	Secondary auditory reaction time task (primary task: driving simulator task)	~500ml	↓	-	-	=
Smit et al. (2004)	28 (ns)	Within-subject	Double blind	Placebo	Simple reaction time task	#250ml	↓	-	-	-
Jay et al. (2006)	15 (8)	Within-subject	None	Control	Psychomotor vigilance task	~500mL	=	-	-	=

Table 5 Continued

Study	*N*[a]	Design[b]	Blinding[c]	Placebo/ Control Condition	Task	Energy Drink Condition[d]	Simple RT[e]	Choice RT[e]	Recognition RT[e]	Accuracy[e]
Howard and Marczinski (2010)	80 (34)	Between-subject	ns (single blind)	Placebo	Cued go/no-go task (mean change in RT)	~1.8mL/kg	-	-	↓^	=
						~3.6mL/kg			↓^	
						~5.4mL/kg			↓^	
Mucignat-Caretta (1998)	12 (6)	Within-subject	ns (single blind)	Placebo	Simple RT task; Go/no-go task	~250mL	=	-	↓^	-
Seidl et al. (2000)	10 (4)	Within-subject	Double blind	Placebo	Simple auditory oddball task	~Capsule	-	-	↓	=

Note. [a] The number in brackets represents the number of male participants. [b] The design is specified based on the energy drink (ED) dosing protocol (between or within subject). [c] Single-blind indicates that participants were blind to treatment condition, double-blind indicates that participants and data collectors were blind to treatment condition, and 'ns' means that blinding was not specified, although in some cases participant blinding can be tentatively inferred from use of a placebo condition. [d] The energy drink (ED) dose was given as a set volume (mL) or calculated according to participant bodyweight (ml/kg); where ~ is indicated, the ED contained 80mg caffeine, 1000mg taurine, and 600mg glucuronolactone per 250mL; where # is indicated the ED contained 75mg caffeine and 100mg taurine per 250mL. [e] These columns indicate whether ED administration significantly (p<.050) increased (↑), decreased (↓), or did not alter (=) reaction or accuracy relative to placebo/control administration, where decreased RT and/or increased accuracy indicates better performance; 'simple RT' tasks involved participants executing a response to the presence of a stimulus (e.g., press the button when the red circle is presented); 'choice RT' tasks involved participants executing distinct responses for each type of stimulus (e.g., press the 'X' key when the red circle is presented and the 'Y' key when the orange circle is presented); 'recognition RT' tasks involved participants executing a response for one type of stimulus and withhold a response for another type of stimulus (e.g., press the button when the red circle is presented but not when the green circle is presented); - indicates that the outcome was not assessed; ^ For these studies a significant effect of ED relative to placebo/control was only recorded in specific conditions: Howard and Marczinski (2010) reported significantly decreased mean RT following ED when invalid (no-go) cues were presented and a trend towards significance (p=.080) for valid (go) cues, and Mucignat-Caretta (1998) found significantly decreased RT after ED administration for females participants and not for male participants. Note that studies reporting on energy beverages that did not contain the three primary ingredients (caffeine, taurine, and glucose/sucrose) were not included in this review. ns: not specified; RT: reaction time.

Table 6

The Effect of ED Ingestion on Simulated Driving Performance

Study	*N*[a]	Design[b]	Blinding[c]	Placebo/ Control Condition	Energy Drink Condition[d]	Task	Speed Deviation[e]	Lane Position Deviation[e]	Steering Wheel Deviation[e]
Gershon et al. (2009)	20 (13)	Within-subject	ns (single blind)	Placebo	~500mL	120 minute drive with minimal changes in road conditions	ns	↓	↓
Horne and Reyner (2001)	11 (6)	Within-subject	Double blind	Placebo	~500ml	120 minute drive following restricted sleep and a 30 minute pre-treatment drive followed by 30 minute break at wheel	-	↓^	-
Mets et al. (2011a)	24 (12)	Within-subject	Double-blind	Placebo	~250ml	120 minute drive following restricted sleep and a 120 minute pre-treatment drive followed by 15 minute break at wheel	↓^	↓	-
Reyner and Horne (2002)	12 (7)	Within-subject	Double-blind	Placebo	~250ml	120 minute drive following restricted sleep and a 30 minute pre-treatment drive followed by 30 minute break at wheel	-	↓^	-

Note. [a] The number in brackets represents the number of male participants. [b] The design is specified based on the energy drink (ED) dosing protocol (between or within subject). [c] Single-blind indicates that participants were blind to treatment condition, double-blind indicates that participants and data collectors were blind to treatment condition, and 'ns' means that blinding was not specified, although participant-blinding can be tentatively inferred from use of a placebo condition. [d] The ED dose was given as a set volume (ml); where ~ is indicated, the ED contained 80mg caffeine, 1000mg taurine, and 600mg glucuronolactone per 250mL. [e] This column indicates whether ED administration significantly ($p<.05$) improved (↑), impaired (↓), or did not alter (=) driving performance relative to placebo/control administration; - indicates that the outcome was not assessed; ^ For these studies a significant effect of ED relative to placebo/control was only recorded in specific conditions: Horne and Reyner (2001) and Reyner and Horne (2002): improvement in driving performance after ED were evident for the first 60 minutes only; Mets et al. (2011a): improvement in driving performance after ED was evident for the first 90 minutes only. Note that Gershon et al. (2009) reported the root mean square of lane position, speed, and steering, Horne and Reyner (2001) and Reyner and Horne (2002) reported the number of lateral lane crossings, and Mets et al. (2011a) reported the standard deviation of lateral lane position and standard deviation speed. Studies reporting on energy beverages that did not contain the three primary ingredients (caffeine, taurine and glucose/sucrose) were not included in this review. ns: not specified

Table 7

The Effect of ED Ingestion on Perceived Fatigue

Study	*N*[a]	Design[b]	Blinding[c]	Placebo/ Control Condition	Energy Drink Condition[d]	Measure	Fatigue Outcome[e]
Gershon et al. (2009)	20 (13)	Within-subject	ns (single blind)	Placebo	~500mL	Swedish Occupational Fatigue-20 Inventory	↓^
Howard and Marczinski (2010)	80 (34)	Between-subject	ns (single blind)	Placebo	~1.8mL/kg ~3.6mL/kg ~5.4mL/kg	Mental fatigue rating scale	↓
Mets et al. (2011b)	24 (12)	Within-subject	Double-blind	Placebo	~250ml	Karolinska Sleepiness Scale	↓
Reyner and Horne (2002)	12 (7)	Within-subject	Double-blind	Placebo	~250ml	Karolinska Sleepiness Scale	↓^

Note. [a] The number in brackets represents the number of male participants. [b] The design is specified based on the energy drink (ED) dosing protocol (between or within subject). [c] Single-blind indicates that participants were blind to treatment condition, double-blind indicates that participants and data collectors were blind to treatment condition, and 'ns' means that it was not specified, although participant-blinding can be tentatively inferred from use of a placebo condition. [d] The ED dose was given as a set volume (ml); where ~ is indicated, the ED contained 80mg caffeine, 1000mg taurine, and 600mg glucuronolactone per 250mL. [e] This column indicates whether ED administration significantly (p<.050) increased (↑), decreased (↓), or did not alter (=) self-reported ratings of fatigue relative to placebo/control administration; ^For these studies a significant effect of ED relative to placebo was only found in certain conditions: Reyner and Horne (2002) decreased fatigue after ED was evident for the first 90 minutes only; Gershon et al. (2009) decreases in fatigue were only evident at the morning assessment time point. Studies reporting on energy beverages that did not contain the three primary ingredients (caffeine, taurine and glucose/sucrose) were not included in this review. ns: not specified.

The severity of these self-reported outcomes is not documented. However, clinical data show a trajectory of increased acute ED exposures cases. Analysis of United States emergency department data revealed a ten-fold increase in visits related to ED use between 2005 (*n*=1,494) and 2007 (*n*=10,068), with rates doubling again by 2011 (*n*=20,783). In 2011, 14,042 cases were due to adverse reactions and 6,090 were due to misuse or abuse, although 42% (*n*=8,652) of these cases involved the combination of EDs with other substances (Substance Abuse and Mental Health Service Administration, 2013). An Australian poison information call centre showed a similar, smaller scale, increase in cases, with 12 ED-related calls in 2004 relative to 65 ED-related calls in 2010 (297 total cases during this period) (Gunja & Brown, 2012). While 46% of cases were related to exposure with other drugs, the symptom profile of recreational ED exposures (*n*=217) reflects the central nervous system disruption reported by ED consumers in non-clinical samples (Table 8).

It should be noted that EDs have also been associated with case reports of more serious adverse side-effects, including deterioration of existing psychiatric illness (Chelben et al., 2008), psychosis (Cerimele, Stern, & Jutras-Aswad, 2010), mania (Machado-Vieira, Iviale, & Kapczinski, 2001), acute suicidality (Szpak & Allen, 2012), tachycardia (Nagajothi, Khraisat, Velaquez-Cecena, & Arora, 2008; Terlizzi, Rocchi, Serra, Solieri, & Cortelli, 2008), reverse stress cardiomyopathy (Kaoukis, Panagopoulou, Mojibian, & Jacoby, 2012), cardiac arrhythmia (Cannon, Cooke, & McCarthy, 2001), cardiac arrest (A. J. Berger & Alford, 2009), hypertension (Argano, Colomba, Di Chiara, & La Rocca, 2012), aneurysm rupture and haemorrhage (Argano et al., 2012), seizures (Iyadurai & Chung, 2007), and anxiety disorder onset (Berigan, 2005). These more serious adverse events have typically

occurred following: (i) recent onset of high ED consumption (i.e., between 3 to 14 ED units of unspecified volume and caffeine content), (ii) concomitant use of other stimulants, and/or (iii) use by sensitive consumers, such as adolescents.

Table 8

Frequency of Most Commonly Reported Symptoms for Recreational Exposures after ED (n=117) and after ED with Alcohol and/or Other Caffeine Products (n=71)

Symptom	**Recreational Exposure: ED Only (%)**	**Recreational Exposure: Alcohol or Other Caffeine Product Co-Ingested (%)**
Palpitations/tachycardia	33	22
Tremor/shaking	30	21
Agitation/restlessness	29	22
Gastrointestinal upset	29	29
Chest pain/ischemia	6	8
Dizziness/syncope	6	9
Paraesthesia	6	3
Insomnia	5	3
Respiratory distress	5	5
Headache	4	3

Original source: Gunja and Brown (2012)

The majority of ED-related acute side-effects have been attributed to particular elements of the ingredient profile, primarily caffeine. As aforementioned, the effect of caffeine is typically dose-dependent, in that large doses (≥ 400mg) may result in poorer cognitive performance and increased anxiety (Attwood et al., 2007; Lorist & Tops, 2003; A. Smith, 2002). Intake of caffeine doses higher than 500mg can result in caffeine intoxication depending on the consumer's tolerance. Regular use of large quantities of caffeine can cause 'caffeinism', a clinical syndrome signalled by

nervousness, restlessness, insomnia, gastrointestinal upset, diuresis, difficulty concentrating, muscular twitching, tachycardia or cardiac arrhythmia, and psychomotor agitation (Griffiths et al., 2003). The onset of these symptoms can occur at lower doses for vulnerable consumers, such as children, pregnant women, and caffeine-naive individuals.

The Australia New Zealand Food Standards Code (Food Standards Australia and New Zealand, 2009) specifies that ED packaging must display warnings to the effect that daily consumption of more than two standard 250mL EDs (160mg caffeine) is not recommended. In Australia, EDs may contain a maximum of 320mg/L caffeine, or 80mg per standard 250mL ED, meaning that EDs have a similar caffeine content to a standard cup of instant coffee (78mg/250mL), and less caffeine than a standard cup of ground coffee (160mg/250mL) (Food Standards Australia and New Zealand, 2009). In contrast, in the United States, EDs can be classified as dietary supplements, circumventing legislation regarding caffeine content and packaging for cola-type soft drinks. As such, EDs can contain up to 505mg/710mL without warning labels regarding the quantity of caffeine or appropriate use of the product (Arria et al., 2013; Reissig et al., 2009), although regulations relating to EDs are currently the focus of scrutiny and potential revision.

2.2.4 Risk-Taking

The ingredient profile of EDs has also been associated with negative behavioural outcomes. Survey research with consumer subgroups has shown that frequency of ED use is significantly and positively associated with: alcohol abuse; tobacco, marijuana, and other illicit drug use; recreational prescription drug use; sexual risk-

taking (failure to use barrier protection, casual sex with a stranger); seatbelt omission while riding in a car; physical violence; risk-taking on a dare; and other alcohol-related consequences (Arria et al., 2010; Miller, 2008a; Miller & Quigley, 2011)[8]. A longitudinal cohort study of a convenience sample of United States university students (*N*=1,060) showed that ED consumption was associated with future recreational use of prescription stimulants and analgesics (Arria et al., 2010)[9]. Data collected from this cohort (*N*=1,097) later during their education showed that high frequency ED users (≥52 days of ED use in the past year) had a two-fold increased odds of meeting alcohol dependence criteria relative to low frequency ED consumers and non-consumers (Arria et al., 2011).

Elevated rates of risk-taking among ED consumers may be a function of systematic individual differences between ED consumers and non-consumers as opposed to the pharmacological effects of the beverage. The characteristic ED consumer profile (i.e., young adult males high in trait impulsivity and sensation seeking) indicates that these beverages may attract a more risky, impulsive consumer (Arria et al., 2010; Arria et al., 2011; L. Berger et al., 2011; Miller & Quigley, 2011). Miller (2008b) argues that ED marketing strategies centred on associations with sport, masculinity, and risk-taking allow consumers to vicariously participate in risky, extreme behaviour through their personal ED use. Thus, it may be that: (i) ED use increases risk-taking behaviour, (ii) people high in risk-taking propensity are attracted to ED use, or (iii) a combination of the two. The relative contribution of pharmacological versus personality, psychological, and environmental factors to ED-related risk-

[8] Miller and Quigley (2011) found that frequency of ED use was not significantly associated with current tobacco use and lifetime illicit drug use after controlling for frequency of other caffeine use.

taking remains unclear; to date, there has been no experimental research conducted objectively assessing the pharmacological effects of ED use on risk-taking.

2.2.5 Energy Drinks: Summary

Consumption of EDs is an increasingly prevalent practice offering functional performance benefits. However, increased stimulation post-ED consumption can have a dual-effect, with self-reported negative physiological and psychological side-effects (e.g., cardiovascular and renal disruption, sleeping difficulties, motor agitation, and increased anxiety and tension) following excess intake or use by individuals who are sensitive to caffeine. In regards to ED behavioural outcomes, consumers typically appear to be individuals with a higher risk-taking propensity, and frequency of ED consumption has been associated with engagement in risk-taking behaviour. However, a paucity of experimental research directly assessing the behavioural consequences of ED consumption limits inferences regarding the pharmacological effects of ED use on behavioural outcomes.

2.3. Alcohol Mixed With Energy Drinks (AmED): An Introduction

2.3.1 Co-Ingestion Defined

As summarised above, it has been widely reported that both alcohol and EDs can be consumed in a manner which has the potential to cause harm. Thus, it logically follows that ingesting a combination of these substances has the potential to also lead to negative outcomes for the consumer. Co-ingestion can be achieved by consuming the two constituents in the one beverage (simultaneous use) or in the same drinking session (subsequent use). Hand-mixed simultaneous AmED use typically comprises 30mL vodka or liqueur (a 'shot') mixed with 125mL or 250mL ED (alcohol/volume 5% to 10%) (Pennay & Lubman, 2012a). These beverages are often 'chugged' or 'skulled' (consumed rapidly without pause) as a 'bomb' drink, where the alcohol shot is dropped into the ED portion immediately prior to consumption (Pennay & Lubman, 2012a). Simultaneous co-ingestion can also be achieved by consuming pre-mixed AmED beverages which are packaged similar to EDs but often comprise less caffeine than a standard ED, and a higher alcohol strength compared to other ready-to-drink beverages (e.g., Pulse®: 31mg caffeine and 7% alcohol/volume) (S. C. Jones, Barrie, & Berry, 2012; Pennay & Lubman, 2012a). Subsequent use is typically defined as consuming the two constituents in separate beverages within two (de Haan et al., 2012) or four hours of one another (Woolsey et al., 2010).

2.3.2 Prevalence of Use

Inferences regarding AmED prevalence are generally based on cross-sectional research in the United States and Europe with high risk populations, typically university students, adolescents, illicit drug users, and patrons of licensed venues

(Table 9). AmED use appears to be a normative practice amongst university students, with between one-quarter and three-quarters of those sampled reporting lifetime AmED use (L. Berger et al., 2013; Marczinski, 2011). The practice of co-ingesting is less common amongst adolescents, with around one-fifth of those surveyed self-reporting past year use (Azagba, Langille, & Asbridge, 2013), and more common amongst illicit drug users, with nearly three-quarters of interviewed regular ecstasy users in Australia reporting AmED use in the past six months (Sindich & Burns, 2011). Estimates of use are the lowest amongst bar patrons, most likely due to the restricted timeframe assessed, with less than one-tenth of those interviewed reporting AmED consumption in the preceding 12 hours (Rossheim & Thombs, 2011; Thombs et al., 2010; Thombs et al., 2011).

Although these studies provide an indication of use amongst high-risk subgroups, it is important to note the variability in estimates of use between studies with similar sample profiles and timeframes for use. This variability may be due to omission of operationalized descriptions of AmED use in several studies, leaving the definition of use open to participant interpretation. It may also be partly due to the lack of standardisation in defining AmED use across studies, particularly as AmED use can be differentially categorised as consumption of pre-mixed beverages, hand-mixed beverages, or a combination of both practices (Table 9).

Table 9

Percentage of AmED Users in Specific Sub-Populations

Study	Year[a]	*N*[b]	Study Details[c]	Sampling[d]	Definition of AmED[e]	AmED Consumers (%)[f]
						Last 12 hours
Rossheim and Thombs (2011)	*2008/2010*	*413 (248*)*	*Structured face-to-face interview and self-administered survey of United States bar patrons exiting licensed venues between 10pm-3am and reporting alcohol consumption (94% under 26 years of age)*	*Convenience*	*Alcohol hand-mixed with ED onsite*	*6**
Thombs et al. (2010)	2008	693 (493)	Structured face-to-face interview and self-administered survey of United States bar patrons exiting licensed venues between 10pm-3am and reporting alcohol consumption (age characteristics for sample ns)	Convenience	Simultaneous	7
				Convenience	Separate (within 12 hours)	7
Thombs et al. (2011)	2010	256 (157*)	Structured face-to-face interview and self-administered survey of United States bar patrons exiting licensed venues between 11pm-2:30am and reporting alcohol consumption (age characteristics for sample ns)	Convenience	Simultaneous	5
						Last fortnight
Marczinski (2011)	2008	706 (354)	Online self-administered survey of United States university students (*M*=20.9, *SD*=5.3 years)	Convenience	'Mixed'; definition not specified	36
						Last week
Price, Hilchey, Darredeau, Fulton, and Barrett (2010)	ns	72 (31)	Standardised structured face-to-face interviews with Canadian university students who identified as past month ED users (17-29 years)	Convenience	Simultaneous use and subsequent use (in one hour)	7*

Table 9 Continued

Study	Year[a]	*N*[b]	Study Details[c]	Sampling[d]	Definition of AmED[e]	AmED Consumers (%)[f]
						Last month
Brache and Stockwell (2011)	2009/2010	465 (205)	Online self-administered survey of Canadian university students (*M*=24 years)	Convenience	Simultaneous use	23
Miller (2012)	ns	648 (340)	Online self-administered survey of United States university students (*M*=20.1, range 18-40 years)	Convenience	Simultaneous use	29
O'Brien et al. (2008)	2006	4721 (1,841)	Online self-administered survey of United States university students (*M*=20.4 years)	Convenience	'Mixed'; definition not specified	24
Oteri et al. (2007)	ns	450 (185)	Paper self-administered survey of Italian university students (*M*=24.5 years)	ns	'Combined use'; definition not specified	48
Snipes and Benotsch (2013)	2011	704 (282*)	Online self-administered survey of United States university students (*M*=19.0, *SD*=1.8 years)	Convenience	Simultaneous use	19
Velazquez et al. (2012)	2009	585 (257*)	Online self-administered survey of United States university students (*M*=18.7 years) who had participated in an alcohol prevention program	Convenience	'Mixed'; definition not specified	15
						Last six months
Azagba et al. (2013)	2011	36,155 (17,439)	Paper self-administered classroom-based Youth Smoking Survey of Canadian school students grade 7 to 12 (age characteristics of sample ns)	Stratified	Simultaneous use (premixed and hand-mixed)	20
L. Berger et al. (2013)	2010	606 (208*)	Face-to-face and online self-administered interviews with United States university students who were participating in a study examining a direct alcohol biomarker (*M*=21.5, *SD*=1.7, range 18-25 years)	Convenience	Simultaneous use (premixed and hand-mixed)	65
Woolsey (2010); Woolsey et al. (2010)	2006	401 (144)	United States university student athletes (*M*=19.8 years; administration method ns)	Convenience	Simultaneous and subsequent use (in two hours)	37
Sindich and Burns (2011)	2010	693 (402)	Interview-administered survey of regular Australian ecstasy users (*M*=24 years)	Purposive	'Mixed'; definition not specified	70

Table 9 Continued

Study	Year[a]	*N*[b]	Study Details[c]	Sampling[d]	Definition of AmED[e]	AmED use (%)[f]
						'Ever' used
L. Berger et al. (2013)	2010	606 (208*)	Face-to-face and online self-administered interviews with United States university students who were participating in a study examining a direct alcohol biomarker (*M*=21.5, *SD*=1.7, range 18-25 years)	Convenience	Simultaneous use (pre-mixed and hand-mixed)	75
Locatelli, Sanchez, Opaleye, Carlini, and Noto (2012)	2008	2,613 (1,254*)	Paper self-administered survey of private school students in São Paulo, Brazil (91.3% aged 15-17 years)	Stratified	'Concomitant use'; definition not specified	32
Marczinski (2011)	2008	706 (354)	Online self-administered survey of United States university students (*M*=20.9, *SD*=5.3 years)	Convenience	'Mixed'; definition not specified	44
Nordt et al. (2012)	2009	2,158 (1,038)	Researcher-administered survey of patients at two San Diego Emergency Departments, United States (28.1% were aged 18-29 years; 48.6% were aged 30-54 years)	Convenience	'Mixed'; definition not specified	6
Price et al. (2010)	ns	72 (31)	Standardised structured face-to-face interviews with Canadian university students who identified as past month ED users (17-29 years)	Convenience	Simultaneous use and subsequent use (in one hour)	76

Table 9 Continued

Study	Year[a]	*N*[b]	Study Details[c]	Sampling[d]	Definition of AmED[e]	AmED use (%)[f]
						Not specified
Ballistreri and Corradi-Webster (2008)	2005	137 (114)	In-class paper self-administered survey of Argentinean physical activity students (*M*=22.6, *SD*=2.3, range 21-38 years)	Convenience	'Mixed'; definition not specified	88
de Haan et al. (2012)	2011	6002 (ns)	Online self-administered survey of Dutch university students (age characteristics of sample ns)	Convenience	Simultaneous use and subsequent use (within two hours)	21*

Note. [a] This column represents the year the data was collected. [b] The figure in parentheses represents the number of male participants; * this number was calculated from details provided in the publication. [c] This column details the method of data collection and sample characteristics, with information regarding age of participants indicated in brackets. [d] This column details the method of sampling; 'stratified' sampling is probability-based, whereby each member within a chosen subset of the population has an equivalent chance of participating; 'convenience' sampling is non-probability based, where participants are selected on the basis of being available and convenient; 'purposive' sampling is non-probability based, where participants are selected based on the purpose of the study. [e] This column denotes the definition of AmED use applied; 'simultaneous' use refers to the consumption of alcohol and EDs mixed in the one beverage either purchased 'pre-mixed' or 'hand-mixed' by the consumer; 'subsequent' use refers to consumption of the two constituents within a specific time period of one another. [f] This column indicates the percentage of the sample who reported AmED use within the time period specified. ns: not specified; AmED: alcohol mixed with energy drink; ED: energy drink.

Another concern with these studies is the targeted recruitment of AmED consumers within the subgroups via convenience sampling. Prevalence studies using nationally representative samples provide a less biased estimate of AmED use in this regard. The 2010 Canadian Alcohol and Drug Use Monitoring Survey, a national telephone survey of 13,615 people over the age of 15, showed that only 2.5% of those who had consumed alcohol in the past month also reported recent AmED use (hand-mixed or pre-mixed); this prevalence increased to one-tenth of the sample (11%) when restricting analyses to the young adult subsample (i.e., 18-24 years) (Brache, Thomas, & Stockwell, 2012). In contrast, higher estimates of use were reported over a longer reference period (i.e., past year as opposed to past month) in a smaller community-based study of 946 residents of Milwaukee (Wisconsin, United States), with 6% of the total sample identifying as AmED consumers (L. Berger et al., 2011). However, these studies may have an issue with undercoverage bias, in that random-digit dialling of landline telephones for participant recruitment may have resulted in underrepresentation of the young adult target AmED age demographic (18 to 35 years), as this sub-population has high rates of cell-phone use (Delnevo, Gundersen, & Hagman, 2008).

2.3.3 Public Policy Response

To date, there have been no community-based or national estimates of AmED use in Australia. However, reports of serious adverse events post-ED and -AmED consumption (e.g., A. J. Berger & Alford, 2009) have prompted a response from peak health professional organisations and regulatory bodies. The Australian Medical Association has released several public alerts highlighting the possible dangers of pre-mixed and hand-mixed AmED consumption and called repeatedly for

a review of ED and AmED marketing, as well as limits on sales (Australian Medical Association, December, 2010, December, 2012, January, 2013). This response has been reflected at the international level. For example, the United States Food and Drug Administration (November, 2010) has also released public alerts regarding caffeinated alcohol consumption, and in the past few years the European Centre for Monitoring Alcohol Marketing (2008), the National Foundation for Alcohol Prevention in the Netherlands (Anderson, 2007), and the Food Safety Promotion Board of the Republic of Ireland (2002) have called for further regulation of EDs and AmED, with several regulatory bodies (Food Standards Agency; Health Canada, 2012) implementing new controls or intermediary actions until an empirical evidence base regarding the harms is established.

In Australia, the Ministerial Council on Drug Strategy has tasked the Intergovernmental Committee on Drugs with developing an urgent action plan to respond to reports of AmED-related harms (Department of Health and Ageing, March, 2011)[10]. With the exception of a ban on licensed venue AmED sales post-midnight in one state of Australia, there have been no public health campaigns or legislative changes in Australia in relation to AmED to date. In order to justify such changes, there must be a solid evidence base indicating that consumers are ingesting AmED in a manner and within a setting that increases the risk for alcohol-related harms. This can be established by examining AmED consumption patterns;

[10] The Ministerial Council on Drug Strategy is the peak policy and decision-making group for the *National Drug Strategy 2010-2015* which aligns law enforcement, health, and education spheres. The Intergovernmental Committee on Drugs is responsible for ongoing work on the *National Drug Strategy 2010-2015* and includes Commonwealth, State and Territory government representatives of health and law enforcement sectors in Australia and New Zealand. This committee is responsible for implementing those policies outlined in the *National Drug Strategy 2010-2015* and providing policy advice to ministers on related issues.

specifically, the frequency and quantity of use, methods for co-ingesting, and drinking context, as well as the motivations driving beverage choice. Furthermore, policy reform must be justified, in that there needs to be a strong body of research showing aggravation or addition of alcohol-related harms following AmED use relative to consumption of alcohol without ED.

Hereafter, this chapter will be dedicated to reviewing the available research and identifying those areas in which there is a lack of research or where the available evidence is equivocal or methodologically limited. The first section will comprise an overview of the available literature regarding AmED consumption patterns and motivations for use. The second section will comprise an overview of the theorised pharmacological interaction between alcohol and ED, and the physiological, psychological, and behavioural consequences of this consumption practice.

2.4 Alcohol Mixed with Energy Drinks: Consumption Patterns and Motivations for Use

2.4.1 Frequency of Use and Quantity of Intake

While the research reviewed in Section 2.3.2 suggests that AmED is a normative practice amongst surveyed university students, the current research with this consumer group indicates that AmED may be less frequently consumed relative to independent use of alcohol or ED. AmED consumers (*n*=132) in a convenience sample of United States university student athletes reported typically ingesting AmED on 0.9 days, alcohol (without EDs) on 1.8 days, and EDs (without alcohol) on 1.3 days per week in the past year (Woolsey et al., 2010). Two other studies have indicated an even lower frequency of AmED use amongst this consumer subgroup. Brache et al. (2012) found that AmED users (*n*=105) in a Canadian university student sample reported hand-mixed or pre-mixed AmED use on approximately two days in the past month. Similarly, Malinauskas et al. (2007) found that nearly three-quarters (73%) of a sample of United States university students identifying as AmED consumers (*n*=253) mixed the beverages while partying on a monthly to weekly basis; only one-tenth (11%) reported using AmED several times per week (≥ 11 days per month). It is important to note here that these studies were restricted to convenience samples of university students, thus restricting generalisability to consumers in the general population.

Despite this lower frequency of use, AmED consumers may still be at increased risk of harms when co-ingesting based on their typical ED intake. As noted in Section 2.2.3, Australian guidelines recommend maximum daily intake of two standard 250mL EDs (160mg caffeine) per day (Food Standards Australia and New Zealand,

2009). However, 61% of AmED consumers (*n*=132) in a convenience sample of United States university student athletes reported that their typical AmED sessions in the preceding year comprised ED 'binges' (≥3 EDs), while only 33% reported 'binges' when consuming EDs without alcohol (Woolsey et al., 2010). This excess intake is not restricted to the ED component of co-ingestion. Research with university student samples indicates that alcohol consumption in AmED drinking sessions typically exceeds Australian recommended maximum intake guidelines of four standard drinks per occasion (National Health and Medical Research Council, 2009), with an average intake of 5.4 to 8.6 standard drinks reported in Dutch, Canadian, and United States university student convenience samples (de Haan et al., 2012; Price et al., 2010; Woolsey et al., 2010). There is contradictory evidence as to whether this intake typically exceeds that reported for alcohol drinking sessions which do not involve ED (see Section 2.6 for a full review of the literature).

Thus, it appears that university students in Europe, Canada, and the United States may be ingesting AmED less frequently, but at more harmful levels, relative to the independent consumption of these constituents; whether these results are generalisable beyond university student consumers and to other geographical regions remains to be seen. Qualitative interviews with Australian adult AmED consumers have provided preliminary evidence that the prevalence of high-risk intake may be lower amongst community samples (Pennay & Lubman, 2012a). In an Australian study, seven of the 10 participants interviewed reported typically restricting their intake to two to five AmED beverages (equivalent to approximately 250 to 625mL ED) per night, while the remaining participants typically consumed between 8 and 12 AmED beverages (equivalent to 1000 to 1250mL ED) per night (Pennay &

Lubman, 2012a). To date, there has been no quantitative research assessing the frequency and quantity of AmED intake at the community level in Australia.

2.4.2 Beverage Choice

Reports of greater ED intake in AmED sessions may be a function of the method of mixing. The majority of university student consumers surveyed report hand-mixed, as opposed to pre-mixed, AmED use. For example, two-fifths (41%) of lifetime AmED consumers (*n*=606) in a United States university student convenience sample reported only using hand-mixed AmED, while 30% used both methods and 5% used premixed AmED (L. Berger et al., 2013). Similarly, only 39% of AmED consumers (*n*=105) in a Canadian university student sample reported consuming pre-mixed AmED in the last month, with the remainder consuming hand-mixed AmED (Brache et al., 2012). Quantification of intake may be simpler when consuming premixed beverages, as hand-mixing may result in variable alcohol and ED volumes per beverage, particularly if venue staff free-pour[11] or if consumers mix without using standardised measurement instruments.

Identifying the typical ED beverages hand-mixed with alcohol is important from a harm reduction perspective, as ED products may differ in their ingredient composition. Previous research with university student convenience samples has shown that the majority of ED consumers report strong brand preference, typically consuming Red Bull® (Attila & Cakir, 2011). This brand preference was reflected in

[11] 'Free-pouring' refers to the practice of measuring liquor by hand based on internal count or cadence as opposed to using a measurement tool.

an Australian qualitative study, with all 10 AmED consumers interviewed identifying Red Bull® as their mixer of choice (Pennay & Lubman, 2012a).

Specific brand preferences also appear to extend to the type of alcohol consumed. Interviewed Australian AmED consumers reported that their typical alcohol mixer comprised vodka or liqueurs which could be 'bombed' with ED (Pennay & Lubman, 2012a). These participants reported generally using 'bomb' AmED drinks to consume alcohol more rapidly based on the premise that it would facilitate intoxication. This practice may lead to greater alcohol intake, as participants reported typically consuming a 'chaser' drink (e.g., beer) immediately after a 'bomb' drink (Pennay & Lubman, 2012a). However, this study reflected the consumption practices of a small, demographically homogeneous, consumer group (*N*=10); to date, there has been no quantitative research indicating whether these findings extend to AmED consumers in the broader community.

2.4.3 Context of Use

Alcohol consumption in public licensed venues has been associated with an increased risk of heavier alcohol intake and alcohol-related aggression (Rossow, 1996; Single & Wortley, 1993; Stockwell, Lang, & Rydon, 1993). Despite concerns of increased alcohol-related harms post-AmED consumption, there is a paucity of research exploring the typical settings for AmED use. The limited research available suggests that consumers are typically using AmED in unlicensed venues; settings of use endorsed by AmED consumers (*n*=105) in a Canadian university student convenience sample included parties (45%), friend's home (32%), school (16%), or home (16%) (Brache et al., 2012). However, approximately two-fifths (38%) of

these consumers reported using AmED in the night-time economy (i.e., licensed pubs, bars, and clubs) (Brache et al., 2012). Whether use in unlicensed venues is unique to the university student drinking culture requires further investigation; legal drinking age restrictions in some countries may theoretically preclude younger university students from entering licensed venues to engage in AmED use. Qualitative interviews with 10 Australian consumers recruited from the regional community showed that both unlicensed and licensed venues (e.g., suburban pubs and urban bars and clubs) were endorsed as setting for use, although the predominance of either setting was not assessed (Pennay & Lubman, 2012a). To date, there has been no quantitative large-scale assessment of settings for AmED use at the general community level.

This paucity of research regarding consumption patterns extends to the typical time of day for ingesting AmED. In the aforementioned qualitative research, seven of the 10 Australian AmED consumers interviewed typically ingested one or two AmED beverages on commencing drinking to provide an early energy boost, followed by a later period of use (typically commencing around midnight) where AmED 'bombs' and ED and vodka mixers were used (Pennay & Lubman, 2012a). Of the remaining three consumers, all reported continuously ingesting AmED throughout the drinking session. Similar patterns of use were reported in focus group interviews with a convenience sample of Australian university students, with premixed AmED reportedly used as a booster at the beginning or towards the end of a drinking session to increase energy (S. C. Jones et al., 2012). Late night-drinking has been associated with increased risk of alcohol-related harms (Rossow, 1996) and, as stated in Section 2.3.3, one state in Australia has prohibited the sale of AmED after midnight in

licensed venues[12]. The aforementioned qualitative studies indicate that AmED use may be more likely at initiation and nearing cessation of a drinking session. However, this data does not indicate the potential impact of implementing time-of-day sales restrictions to minimise AmED intake and the risk of subsequent alcohol-related harms.

2.4.4 Motivations for Use

As noted above, qualitative research indicates that some consumers use AmED with the intention of facilitating intoxication and increasing alcohol intake (Pennay & Lubman, 2012a). Two studies have assessed whether these motivations are reflected more broadly amongst larger samples[13]. In a study by O'Brien et al. (2008), AmED consumers (*n*=697) in a sample drawn from 10 United States universities reported that the primary motivations for consuming AmED were to hide the flavour of alcohol (55%), to feel and look less drunk (15% and 5%, respectively), and to avoid a hangover (7%). The use of sweetened mixers is a common concern in regards to adolescent and young adult alcohol consumers, as it is argued that the masking effect of the 'sugary sweet' beverages encourages increased alcohol consumption (Chikritzhs et al., 2009; Mart, 2011). The authors of the above study noted that 41% of consumers provided other reasons for AmED use (e.g., 'it was being served at a party') however the nature and frequency of these motivations were not identified, as the focus of this report was on intoxication-related motives.

[12] It should be noted that AmED consumption is still possible, as the ban pertains only to hand-mixing AmED simultaneously; there are no prohibitions regarding the sale of ED and alcohol as independent beverages.

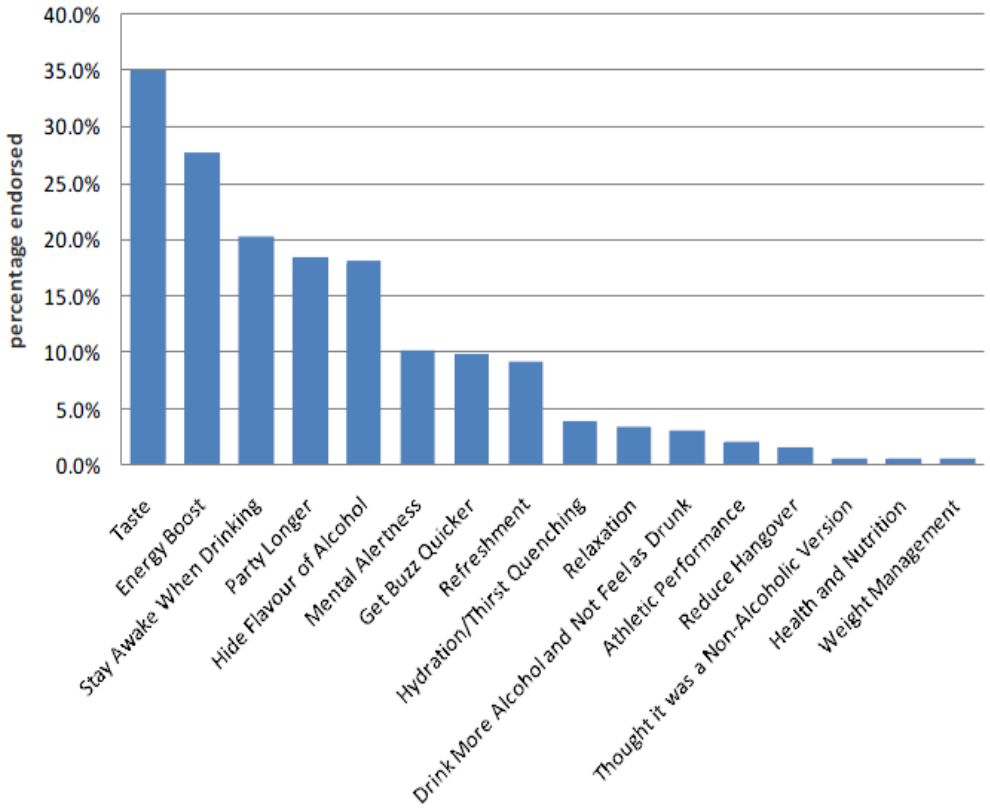

Figure 1. Proportion of University of Victoria (Canada) students endorsing motivations for using caffeinated alcoholic beverages, 2010. Original source: Brache et al. (2012)

In contrast, a more comprehensive assessment of university students' motivations for use indicated that AmED users (*n*=465) in a Canadian university student convenience sample were more likely to endorse the taste (35%) and increased energy after consumption (27%) as a reason for use. However, approximately one-fifth used AmED to facilitate intake: specifically, to stay awake while drinking (20%), to party longer (18%), and to hide the flavour of alcohol (18%) (Figure 1; Brache et al., 2012). These motivations are potential causes for concern; longer drinking periods may increase the likelihood of late-night drinking which, as previously noted, is a risk factor for alcohol-related harms (Rossow, 1996; Single & Wortley, 1993; Stockwell et al., 1993).

Another quantitative survey study of AmED use motivations amongst university students has been conducted by Marczinski (2011), with participants using a 4-point Likert scale (1 'highly disagree' to 4 'highly agree') to indicate their level of agreement with specified motivations. Greatest agreement was evident for items related to AmED-induced fatigue-reduction, enhanced intoxication, and increased alcohol intake; these means scores were all significantly higher than the null score of 2.5. However, treating Likert ordinal data as interval-level measurement assumes that intervals between categories are equal, and that the intensity of feeling between two categories (e.g., 'highly disagree' and 'slightly disagree') is equivalent to the intensity of feeling between other consecutive categories (e.g., 'slightly disagree' and 'slightly agree'). Consequently, this data may not clearly elucidate the relative contribution of these motivations in determining AmED beverage choice.

Overall, this body of literature indicates that there may be a small proportion of consumers using AmED with the intention of enhancing intoxication by: (i) reducing fatigue and increasing the drinking period, (ii) masking the flavour of alcohol with the sweet, palatable taste of ED, and (iii) reducing the impairing effects of drunkenness and facilitating a more desirable intoxication state. However, the prevalence of these motivations across consumers cannot be concluded at present for two reasons. Firstly, previous research has indicated that drinking motives may be partially determined by the drinking culture (Kuntsche, Knibbe, Gmel, & Engels, 2006). As the current research has been restricted to university student samples, it is not possible to draw inferences regarding the motives for AmED consumption in the broader community. The current focus on United States and Canadian samples restricts generalisability to Australian consumers in light of the distinctive drinking

cultures; while 20.1% of Canadian total adult population were classified as current heavy episodic drinkers in 2001-2002, only 13.4% of the Australian population fell within this category (World Health Organisation, 2004)[14].

Secondly, the existing research has only assessed a select range of motivations predominantly related to intoxication enhancement and intake, despite previous research which shows a range of motivations for alcohol consumption, including social (e.g., to be sociable, to enhance social confidence), coping (e.g., to regulate stress, to reduce stress), and conformity (e.g., to gain peer acceptance or as a response to peer pressure) motives (Kuntsche, Knibbe, Gmel, & Engels, 2005). Two small-scale qualitative studies have indicated that these factors may play a role in AmED beverage choice, with Australian consumers reporting use of AmED 'bombs' in a group setting to enhance social status, increase social bonding, and facilitate a sense of belonging (S. C. Jones et al., 2012; Pennay & Lubman, 2012a). Situational factors, such as increased availability, greater convenience, widespread advertising, and frequent drink-discounting, have also been implicated in AmED beverage choice (S. C. Jones et al., 2012; Pennay & Lubman, 2012a). However, these studies reflect the drinking motives of small homogeneous subsamples of Australian consumers (N=10 to 21); no research has been undertaken comprehensively assessing the motivations for AmED use at the community level.

[14] It should be noted that the Canadian estimate reflected the proportion of heavy episodic drinkers amongst those reporting alcohol use, with heavy episodic drinking defined as consumption of five or more drinks on one occasion at least once per month in the last year. In contrast, the Australian estimate was based on the proportion of heavy drinkers in the general population, with heavy episodic drinking defined as consumption of seven/five or more standard drinks for males/females on one occasion at least once per month (World Health Organisation, 2004).

2.4.5 Consumption Patterns and Motivations for Use: Summary

Preliminary evidence suggests that university students ingest AmED less often than alcohol or ED. However, they tend to exceed recommended maximum daily ED intake guidelines, consuming more EDs during AmED sessions relative to when consuming EDs without alcohol. This excess intake may be a function of the predominant method of co-ingesting, with quantification of intake more challenging when consuming hand-mixed as opposed to pre-mixed beverages. This is particularly concerning considering the popularity of 'bomb' drinks which are rapidly ingested with the intention of increasing intoxication. However, these drinking practices may be unique to the drinking culture, as research is limited to university student consumer samples or small community-based samples (i.e., ≤ 21 participants). Furthermore, there is very limited information about the typical context of use, particularly the common time-of-day for ingesting AmED. Clarification of AmED drinking practices (i.e., intake, beverage choice, setting, and time of use) at the community level could inform the development of harm minimisation approaches, particularly in regards to placing limits on the hours of trading for AmED beverages in licensed venues.

Identification of the primary motives for AmED consumption can also provide an evidence base for harm minimisation endeavours in regards to: (i) regulation of AmED sales and marketing in licensed venues, and (ii) consumer education regarding the effects of AmED. Two studies have shown that a subset of surveyed university students use AmED to enhance intoxication; specifically, to reduce fatigue and lengthen the drinking period, mask the flavour of alcohol, and reduce the impairing effects of drunkenness and facilitate a more stimulated intoxication state.

However, the extent to which these motivations extend beyond the university student drinking culture to consumers in the general community has not been examined. Furthermore, there has been no comprehensive assessment of the motives for use; past research has primarily been focused on assessing intoxication-related motives, despite qualitative research implicating social and situational factors in beverage choice.

In order to address this lack of research, the following questions must be addressed:

- What are the consumption patterns associated with AmED use at the community-level in regards to: (i) the frequency and quantity of intake, (ii) drink preferences, and (iii) consumption context?
- What are the primary motivations driving AmED beverage choice at the community level?

2.5 Alcohol Mixed with Energy Drinks: Interaction between the Two Constituents

2.5.1 Theorised Interaction between Alcohol and Energy Drinks

As noted in Section 2.3.4, a subset of AmED consumers report combining alcohol and ED with the intention of facilitating a more stimulated intoxication state. This hypothesis regarding oppositional global pharmacological effects of AmED is logical: EDs typically facilitate cognitive performance and alertness (Section 2.2.2), while alcohol typically impairs cognitive performance, with increased sedation-like effects (Section 2.1.2). Consequently, it has been theorised that the stimulant effects of ED may mask the sedation effects of alcohol when co-ingested (Ferreira et al., 2006); the research regarding this change to the nature of intoxication is reviewed in Section 2.6. This state of intoxication may impair AmED consumers' ability to accurately estimate their intoxication. Specifically, consumers may underestimate their level of intoxication relative to if they had consumed the same amount of alcohol without ED.

In order to demonstrate AmED-induced reduced perception of intoxication, consumers should show: (i) equivalent outcomes on objective measures of intoxication (i.e., BrAC/BAL), and (ii) lower ratings on subjective measures of intoxication (i.e., self-report of perceived intake or level of 'drunkenness'), after AmED relative to alcohol. Previous research on the interaction between alcohol and caffeine, the primary psychoactive ED ingredient, shows mixed support for this premise (Table 10). In contrast with hypothesised outcomes, several studies have revealed equivalent subjective and objective intoxication outcomes following ingestion of alcohol independently or combined with caffeine (Azcona, 1995; Rush,

Higgins, Hughes, Bickel, & Wiegner, 1993). However, Fillmore, Roach, and Rice (2002) found that co-ingestion of a high caffeine dose (4.0mg/kg) with alcohol (mean peak BrAC .079%) significantly increased intoxication ratings, while Marczinski and Fillmore (2006) reported that co-ingestion of a moderate caffeine dose (2.0mg/kg) with alcohol (mean peak BrAC .084%) tended to decrease intoxication ratings, relative to administration of alcohol without caffeine. The latter result was not apparent when participants co-ingested a high caffeine dose (4.0mg/kg). In both studies, caffeine-induced alterations in perceived intoxication were evident even though participants evidenced equivalent objective intoxication (BrAC).

Despite the equivocal nature of the caffeine and alcohol literature, there have only been three studies published to date directly assessing the interactive effects of alcohol and ED on objective and subjective intoxication (Table 11). These studies have consistently shown equivalent BrAC and ratings of intoxication regardless of whether alcohol (mean peak BrAC .043% to .089%) was consumed alone or with ED (approximately 125mL to 250mL ED; 40mg to 80mg caffeine per standard 70kg person) (Marczinski et al., 2011; Marczinski et al., 2012, 2013). The ED doses administered had a lower caffeine content than that administered in those studies showing an interactive effect of caffeine and alcohol (140 to 280mg caffeine per standard 70kg person; Marczinski & Fillmore, 2006). Furthermore, the ED doses administered falls below the retrospective self-reported typical intake reported by AmED consumers (two and three standard 250mL EDs; Section 2.4.1). Given the doses of ED reported as being consumed in survey research, higher ED doses, particularly those which match or exceed the Australian recommended maximum

daily intake guidelines (i.e., two standard 250mL EDs; 160mg caffeine), need to be administered in experimental research to maximise generalisability to real-life consumption.

Secondly, the caffeine and alcohol literature indicates that interactive effects for subjective intoxication may be dose-dependent (Marczinski & Fillmore, 2006). Based on the assumption of caffeine as the primary psychoactive ED ingredient, it may be appropriate to hypothesise that the interactive effect of alcohol and ED for objective intoxication may also be dose-dependent. Research has shown that ingesting alcohol with a sugar-sweetened mixer containing glucose and sucrose, some of the primary ingredients in EDs, significantly decreases BrAC compared to alcohol co-ingested with artificial-sweetened mixers (Marczinski & Stamates, 2013; Rossheim & Thombs, 2011; Wu et al., 2006). Thus, it may be that objective intoxication decreases with increased naturally-sweetened ED administration, due to greater sugar intake. However, the past AmED research has only involved administration of a single ED and alcohol dose, meaning that differential interactive effects according to dose remain unexplored.

Table 10

The Effect of Caffeine on Objective Intoxication (Breath or Blood Alcohol Concentration) and Subjective Intoxication after Alcohol Administration

Study[a]	***N***[b]	**Design**[c]	**Blinding**[d]	**Placebo**	**Subjective Intoxication Measure**	**Alcohol Dose**[e]	**Objective Intoxication BrAC (%)**[f]	**Caffeine Dose**[g]	**Subjective Intoxication Comparison**[h]	**Objective Intoxication Comparison**[h]
Fillmore et al. (2002)	42 (23)	Between-subject	Single-blind#	Placebo	VAS rating of 'drug effect'	0.65g/kg	.079	4.0mg/kg	↑^	=
Howland et al. (2010)	127 (67*)	Between-subject	Double-blind	Placebo	Self-estimate of BAC	.120%	.120	*M*=383mg	=	=
Liguori and Robinson (2001)	15 (6)	Within-subject	Double-blind	Placebo	VAS rating of 'drug effect'	0.6g/kg	.085	200mg	=	=
								400mg	=	=
Marczinski and Fillmore (2003a)	12 (6)	Within-subject	Double-blind	Placebo	Rating of beverage intake	0.65g/kg	.102	2.0mg/kg	=	=
								4.0mg/kg	=	=
Marczinski and Fillmore (2006)	12 (6)	Within-subject	Double-blind	Placebo	Rating of beverage intake	0.65g/kg	.084	2.0mg/kg	↓	=
								4.0mg/kg	=	=
Rush et al. (1993)	8 (7)	Within-subject	Double-blind	Placebo	VAS rating of 'drunkenness'	0.5g/kg	~.040	250mg/70kg	=	=
								500mg/70kg	=	=
						1.0g/kg	~.110	250mg/70kg	=	=
								500mg/70kg	=	=

Note. [a] This table only includes those studies which have included a measure of subjective intoxication (i.e., rating of perceived intake or level of intoxication) and assessment of objective intoxication (i.e., breath alcohol concentration or blood alcohol level); those studies assessing only one outcome, or a variation of the outcome (e.g., perceived impairment) were not included. [b] The number in brackets represents the number of male participants; * the number was calculated according to percentages provided in the manuscript. [c] The design is specified based on the alcohol and caffeine dosing protocol (between or within subject). [d] Single-blind indicates that participants were blind to treatment condition, double-blind indicates that participants and data collectors were blind to treatment condition, and 'ns' means that blinding was not specified; note that # indicates that the study assessed the effects of expectancy, and thus all participants were informed they would receive alcohol, and some were accurately informed about receiving caffeine. [e] The alcohol dose was calculated according to participant body weight (g/kg) or according to a target breath alcohol concentration (% BrAC). [f] This figure reflects the peak mean BrAC recorded for the study (overall or within a condition); note that figures indicated with ~ are estimates based on blood alcohol levels. [g] The caffeine dose was either given as a set dose or calculated according to body weight (mg/kg). [h] This column indicates whether alcohol and caffeine co-administration significantly ($p<.050$) increased (↑), decreased (↓), or did not alter (=) objective intoxication (BrAC) or subjective intoxication relative to administration of alcohol without caffeine; ^ In this study: Fillmore et al. (2002) reported increased perceived intoxication after caffeine and alcohol regardless of whether they were lead to expect that caffeine reduced or did not alter alcohol impairment, relative to placebo, although breakdown analyses showed that those who received caffeine reported greater intoxication than those who did not receive caffeine. ns: not specified; VAS: 100-mm visual analogue scale.

Table 11

The Effect of Energy Drink (ED) on Objective Intoxication (Breath or Blood Alcohol Concentration) and Subjective Intoxication after Alcohol Administration

Study[a]	*N*[b]	Design[c]	Blinding[d]	Placebo	Subjective Intoxication Measure	Alcohol Dose[e]	Objective Intoxication BrAC (%)[f]	Energy Drink Dose[g]	Subjective Intoxication Comparison[h]	Objective Intoxication Comparison[h]
Marczinski et al. (2011)	56 (28)	Between-subject	Double-blind	Placebo	Rating of beverage intake	0.65g/kg	.089	~3.57mL/kg	=	=
Marczinski et al. (2012)	18 (9)	Within-subject	Double-blind	Placebo	Rating of beverage intake	0.65g/kg	.071	~3.57mL/kg	=	=
Marczinski et al. (2013)	80 (40)	Between-subject	Double-blind	Placebo	Rating of beverage intake	1.82mL/kg	.043	~0.91mL/kg	=	=

Note. [a] This table only includes those studies which have included a measure of subjective and objective intoxication; those studies assessing only one outcome, or a variation of the outcome (e.g., perceived impairment) were not included. [b] The number in brackets represents the number of male participants. [c] The design is specified based on the alcohol and ED dosing protocol (between or within subject). [d] Double-blind indicates that participants and data collectors were blind to treatment condition. [e] The alcohol dose was calculated according to participant body weight (g/kg or mL/kg). [f] This figure reflects the peak mean BrAC recorded in the study (overall or within a condition). [g] The energy drink dose was calculated according to body weight (mL/kg); where ~ is indicated, the ED contained 80mg caffeine, 1000mg taurine, and 600mg glucuronolactone per 250mL. [h] This column indicates whether alcohol and ED co-administration significantly ($p<.050$) increased (↑), decreased (↓), or did not alter (=) objective intoxication (BrAC) or subjective intoxication relative to administration of alcohol without ED. ns: not specified; BrAC: breath alcohol concentration.

2.5.2 Theorised Interaction between Alcohol and Energy Drinks: Summary

In sum, it is theorised based on the pharmacodynamics of alcohol and EDs that co-ingestion may result in oppositional global pharmacological effects, whereby the sedation-based effects of alcohol which may signal level of intoxication are masked by the stimulant effects of ED. This altered intoxication state may lead consumers to underestimate their level of intoxication relative to when consuming alcohol without EDs. For this premise to hold true, consumers should evidence equivalent objective intoxication while showing reduced subjective ratings of intoxication after consuming AmED relative to alcohol. Research examining the interactive effects of alcohol with caffeine shows mixed support for this theory. In contrast with predictions, the small body of AmED literature consistently indicates equivalent outcomes on objective and subjective intoxication after AmED and alcohol administration. However, the three AmED studies published to date directly assessing perceived intoxication have all involved a single low ED dose. The paucity of research adopting higher, and more complex, dosing protocols restricts generalisability to real-life consumption and precludes inferences regarding dose-dependent interactive effects of AmED.

In order to determine whether AmED causes consumers to underestimate their level of intoxication, the following questions must be examined:

- Based on the premise that AmED reduces perceived intoxication, are any changes in objective intoxication (BrAC) and subjective intoxication (ratings of perceived intoxication) evident when comparing the effects of alcohol alone and in combination with a high acute dose of ED (two or more standard 250mL EDs) in a controlled environment for the same individual?

- Following from *Question 6.1*, do objective and subjective intoxication outcomes differ dose-dependently according to the volume of ED co-administered with alcohol?

‘High Risk?’ A Systematic Review of the Acute Outcomes of Mixing Alcohol with Energy Drinks

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Peacock, A., Pennay, A., Droste, N., Bruno, R., & Lubman, D. I. (under review; commissioned). ‘High risk’? A systematic review of the acute outcomes of mixing alcohol with energy drinks. *Addiction*.

2.6 Consequences of Using Alcohol Mixed with Energy Drinks

2.6.1 Preface

As aforementioned, it is theorised that AmED consumption results in increased stimulation and decreased sedation relative to alcohol consumption, the consequence of which may be reduced perception of intoxication. The majority of concerns regarding AmED use have centred on the potential physiological, psychological, and behavioural consequences of co-ingestion. Specifically, these concerns relate to whether AmED consumption causes: (i) increased rates of stimulation-based adverse physiological and psychological side-effects, as a consequence of the stimulation-based effects of ED, and (ii) increased engagement in hazardous drinking practices and risky behaviour, as a consequence of AmED-induced reduced perception of intoxication (Figure 2).

The following manuscript comprises a systematic review of the available research assessing these questions. The specific aims of this review were to clarify whether AmED, relative to alcohol alone: (i) increases the likelihood of physiological and psychological stimulation-based side-effects and decreases the odds of sedation-based side-effects, (ii) increases the likelihood of greater alcohol intake and hazardous drinking practices, and (iii) increases the likelihood of risk-taking behaviour[15].

[15] It should be noted that this review was undertaken in the final term of candidature. As such, the manuscripts comprising Chapters 3, 4, and 6 are reviewed within the manuscript.

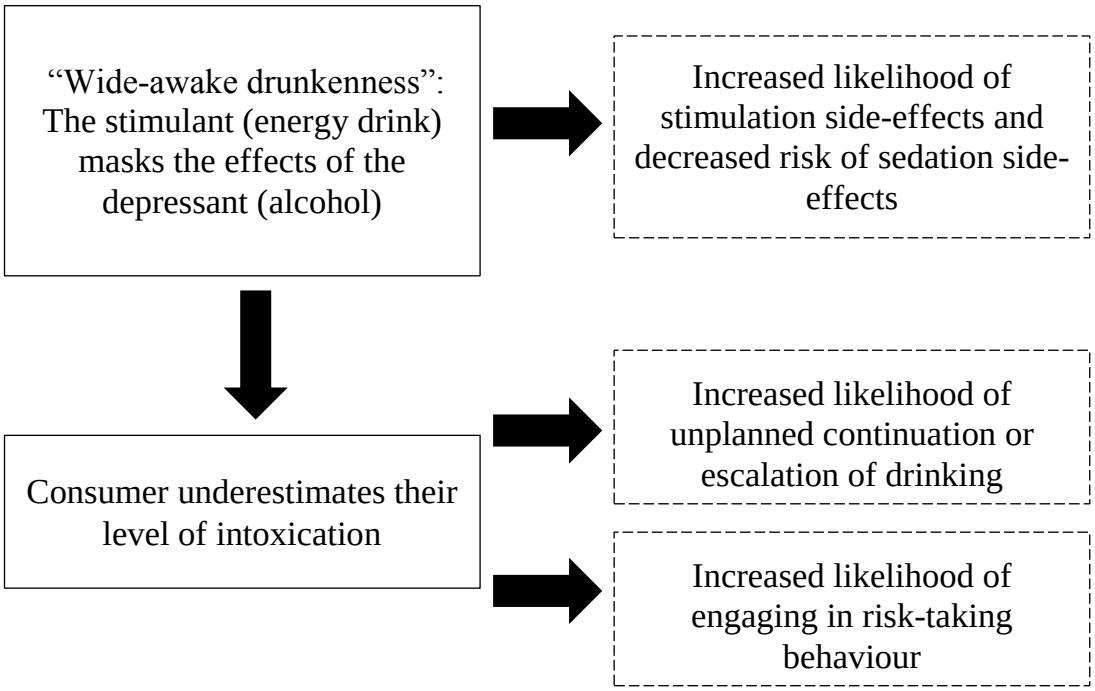

Figure 2. Theorised interaction between alcohol and energy drinks, including the potential consequences of changes to the nature and intensity of intoxication. Those emphasised with a dashed line will be the focus of the following review.

2.6.2 Abstract

Aims: Alcohol mixed with energy drinks (AmED) is a relatively new consumption trend generating increasing concern regarding potential adverse effects. Despite the political and health imperative, there has been no formal synthesis of the literature to determine whether AmED offers additional harms relative to alcohol. The aim of this study was to determine whether co-consumption of energy drinks and alcohol, relative to alcohol alone, alters: (i) physiological, psychological, cognitive, and psychomotor outcomes, (ii) hazardous drinking practices, and (iii) risk-taking behaviour.

Methods: PubMed, PsycINFO, and Embase databases were searched up until May 2013 for articles outlining descriptive, observational analytic, and human experimental studies which compared target outcomes for AmED versus alcohol consumers (between-subjects), or AmED versus alcohol consumption (within-subjects). Odds ratios were calculated for target outcomes following screening, data extraction, and quality assessment.

Results: Data were extracted from 19 articles. Analyses typically revealed increased odds of stimulation-based outcomes and decreased odds of sedation-based physiological and psychological outcomes after AmED relative to when alcohol was consumed alone. AmED consumers generally reported more hazardous alcohol consumption patterns and greater engagement in risk-taking behaviour than alcohol consumers. The within-subjects odds of hazardous alcohol consumption in AmED versus alcohol drinking sessions were equivocal across studies. In contrast, two studies showed lower odds of risk-taking behaviour for AmED relative to alcohol drinking sessions.

Conclusions: Mixing alcohol with energy drinks may exert a dual effect, increasing stimulation-based effects and reducing sedation-based outcomes; the clinical severity and dose threshold is yet to be established. The literature is divergent regarding whether these changes in the nature of intoxication translate into greater alcohol intake and risk-taking behaviour.

2.6.3 Introduction

The consumption of alcohol mixed with energy drinks (AmED) is a recent phenomenon, and concerns have been raised regarding its association with increased alcohol-related harms (Pennay, Lubman, & Miller, 2011). Studies targeting adolescents and young adults, key risk groups for hazardous drinking, indicate widespread use (23%-48% reporting recent AmED use) (Brache & Stockwell, 2011; Oteri et al., 2007). Among these subgroups, some consumers report combining alcohol with energy drinks (EDs) to facilitate a more positive intoxication experience and reduce the sedating effects of alcohol (O'Brien et al., 2008). This assumption of oppositional behavioural effects is logical based on constituent pharmacodynamics. Energy drinks (EDs) alone typically facilitate performance and increase self-reported alertness and stimulation. In contrast, alcohol typically impairs performance, with self-reported increases in sedation. It has been theorised that the stimulant effects of EDs mask the depressant effects of alcohol, reducing physiological and psychological sedation-based effects (e.g., fatigue), while increasing stimulation (e.g., alertness, energy) (Ferreira et al., 2006; Marczinski et al., 2011). This state of intoxication, which has been referred to as ‘wide-awake drunkenness’ (Arria & O'Brien, 2011), may impair consumers’ ability to estimate intoxication. While the evidence-base supporting this premise has been challenged (Verster, Aufricht, & Alford, 2012), AmED-induced underestimation of intoxication has been linked to behavioural changes, specifically: (i) more hazardous drinking practices and (ii) poorer risk assessment and increased risk-taking behaviour (Weldy, 2010). These behavioural changes increase the possibility of additional alcohol-related harms.

AmED research has expanded rapidly following increasing recognition of these potential harms. However, there has been no formal systematic synthesis of the literature to determine whether AmED poses additional harms relative to alcohol. An integration of the literature is timely from a political and health standpoint (Australian Medical Association, January, 2013; United States Food and Drug Administration, November, 2010), with several countries currently developing policy responses to AmED (e.g., Brache et al., 2012; Department of Health and Ageing, March, 2011). As such, the primary objective of this article is to systematically review AmED research to determine whether co-consumption of energy drinks and alcohol poses additional harms relative to alcohol alone for: (i) physiological, psychological, cognitive, and psychomotor outcomes, (ii) hazardous drinking practices, and (iii) risk-taking behaviour.

2.6.4 Method

2.6.4.1 Search Strategy

The study selection and data extraction process were outlined in a protocol prior to commencement (Appendix A). Studies were identified by author AP[1] via PubMed, PsycINFO, and Embase (last search May 8, 2013). Each ED-related search term ("*energy drink*", "Red Bull")* was combined with the term *alcohol**, entered in conjunction with: *risk**, *behavio**, *adverse**, *effect**, *harm**, *health**, *excess**, *consum**, *intake** (Appendix B: example search strategy). AP[1] removed duplicates and completed initial eligibility screening based on publication criteria. Content assessment (based on title/abstract) was performed by AP[1] and ND using a standardised template; assessment was not blind, with full-text revision where

necessary. Disagreement between reviewers regarding exclusion occurred for 15.1% of articles (*n*=8); disagreements were resolved by consensus.

2.6.4.2 Inclusion/Exclusion Criteria

2.6.4.2.1 Publication Criteria

Studies adopting descriptive, observational analytic, and human experimental designs were included; animal studies, case studies, qualitative papers, reviews, methodology papers, and commentaries were excluded. Peer-reviewed journal articles published in English between January 1990 and May 2013 with the search terms in title/abstract were included.

2.6.4.2.2 Content Criteria

AmED use was defined as consumption of: (i) pre-mixed beverages, (ii) hand-mixed beverages, or (iii) separate beverages in the same drinking session. EDs were defined as functional beverages which contain caffeine, sugars, and taurine; other ingredients may include glucuronolactone, B vitamins, and herbal extracts (Pennay et al., 2011).

As the objective was to examine the relative likelihood of harms after AmED and alcohol, studies were included if they included comparison of AmED versus alcohol consumers (between-subjects), or AmED versus alcohol consumption (within-subjects) in regards to: (i) physiological, psychological, cognitive and psychomotor outcomes, (ii) alcohol consumption and alcohol priming, and/or (iii) risk-taking behaviour.

2.6.4.3 Data Extraction

A data extraction sheet, piloted on five random studies, was used by AP^1 and AP^2 to extract the following information: study aim, design, sample characteristics, sampling method, primary measures, method of administration, outcomes, conclusions, limitations, funding, and conflicts of interest. The Joanna Briggs Institute Critical Appraisal Checklist for Descriptive Studies (Joanna Briggs Institute, 2011), Joanna Briggs Institute Critical Appraisal Criteria for Cohort/Case-Control Studies (Joanna Briggs Institute, 2011), and the Cochrane Collaboration tool (Higgins et al., 2011) were used for quality assessment. Data was requested from authors for seven studies (Ferreira et al., 2006; Ferreira, de Mello, Rossi, & Souza-Formigoni, 2004; Marczinski et al., 2011; Marczinski et al., 2012, 2013; O'Brien et al., 2008; Thombs et al., 2010). Disagreement on any of the key data extracted was resolved by discussion, with a final decision by ND where no consensus was reached. While no studies were removed based on quality assessment, these outcomes were qualitatively considered in the synthesis.

Odds ratios (OR) were calculated based on reported descriptive and inferential statistics. Correlation between paired comparisons was estimated as .050 unless otherwise specified. Outcomes were grouped within each theme area as: (i) self-reported drinking outcomes in natural scenarios (retrospective or prospective) for (a) AmED versus alcohol consumers, and (b) AmED versus alcohol sessions, (ii) self-reported outcomes of AmED versus alcohol administration in laboratory-based settings, and (iii) objective outcomes of AmED versus alcohol administration in laboratory-based settings.

2.6.5 Results

2.6.5.1 Sample for Synthesis

Eighty-seven articles were retrieved after duplicate removal (Figure 1). Nineteen studies were included in the final sample following exclusion (Table 1).

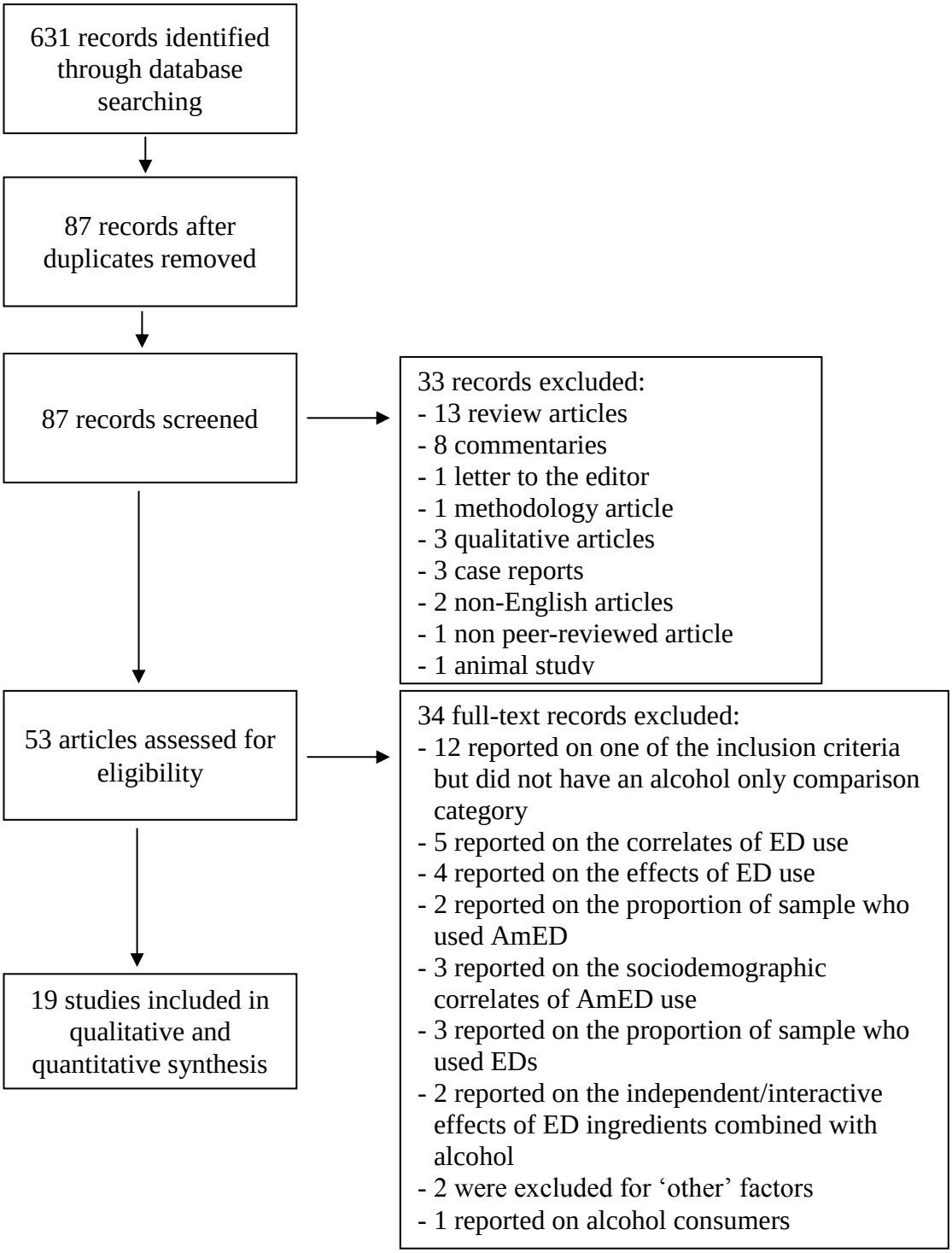

Figure 1. Flow diagram of the number of records included at the identification, screening, eligibility, and synthesis stages.

Table 1

Characteristics of Included Studies (N=19)

Study	Study Design[a]	Method	Sample *N*[b]	Sample Characteristics
Brache and Stockwell (2011)	Cross-sectional descriptive[# ^]	Online self-administered survey	465 *ALC=305* *AmED=105*	Canadian university student convenience sample (*n*=205* males; *M*=20.0, *SD*=6.7, range 17-51 years)
de Haan et al. (2012)	Cross-sectional descriptive[# ^]	Online self-administered survey	4424 *ALC=3185* *AmED=1239*	Dutch university student convenience sample (Alcohol consumers: *n*=1438* male; *M*=22.1, *SD*=2.6 years; AmED consumers: *n*=1730*; *M*=21.5, *SD*=2.3 years)
O'Brien et al. (2008)	Cross-sectional observational[#]	Online self-administered survey	4237 *ALC=2189* *AmED=697*	United States university student convenience sample (*n*=1638 males; *M*=20.4, *SD*=2.8 years)
Peacock, Bruno, and Martin (2012)	Cross-sectional descriptive[^]	Online self-administered survey	408	Australian community convenience sample who reported AmED use (*n*=159* males; *M*=23.1, *SD*=3.8, range=18-35 years)
Peacock, Bruno, and Martin (2013a)	Cross-sectional descriptive[^]	Online self-administered survey	408	Australian community convenience sample who reported AmED use (*n*=159* males; *M*=23.1, *SD*=3.8, range=18-35 years)
Penning et al. (2011)	Cross-sectional descriptive[#]	Online or paper self-administered survey	549 *ALC=480* *AmED=24*	Dutch university student convenience sample (*n*=177 males; *M*=20.4, *SD*=3.5 years)
Price et al. (2010)	Cross-sectional descriptive[^]	Semi-structured standardised face-to-face interviews	72 *AmED=10*	Canadian university student convenience sample who reported ED use (*n*=31 males; range 17-29 years)

Table 1 Continued

Study	Study Design[a]	Method	Sample *N*[b]	Sample Characteristics
Rossheim and Thombs (2011)	Cross-sectional observational #	Re-analysis of data from Thombs et al. (2010); Thombs et al. (2011)	413 *ALC=326* *AmED=25*	United States college bar exiting patron convenience sample; inclusion required alcohol consumption that night (*n*=253* males; whole sample age ns)
Thombs et al. (2011)	Cross-sectional observational #	Structured face-to-face interview; self-administered pen and paper questionnaire	256 *ALC=180* *AmED=10*	United States college bar exiting patron convenience sample; inclusion required alcohol consumption that night (*n*=157* males; whole sample age ns)
Thombs et al. (2010)	Cross-sectional descriptive #	Structured face-to-face interview; self-administered pen and paper questionnaire	697 *ALC=602* *AmED=45*	United States college bar exiting patron convenience sample; inclusion required alcohol consumption that night (whole sample sex/age ns)
Woolsey et al. (2010)^	Cross-sectional descriptive # ^	Survey (administration method ns)	401 *ALC=165* *AmED=150*# *AmED=132*^	United States university student athlete convenience sample (*n*=257 males; *M*=19.8, range 18-23 years)
Woolsey (2010)^	Cross-sectional descriptive # ^	Re-analysis of data from Woolsey et al. (2010)	401 *ALC=165* *AmED=150*	United States university student athlete convenience sample (*n*=257 males; *M*=19.8, range 18-23 years)
Alford, Hamilton-Morris, and Verster (2012)	Human experimental mixed #	Double-blind placebo-controlled multi-dose administration of 250mL ED or 0mL ED with alcohol (intended peak BAC .046% and 0.1%), and placebo alcohol (peak mean BrAC drink 1=.047%; drink 2=.094%)	20	Healthy regular alcohol consumers who had tried an ED before recruited from the general community (*n*=10 males; *M*=24.5, range 19-33 years)
Ferreira et al. (2004)	Human experimental crossover ^	Double-blind placebo-controlled administration of: (i) placebo, (ii) 1.0/kg alcohol, (iii) 3.57mL/kg ED, and (iv) AmED (peak mean BrAC ns)	14	Healthy moderate male alcohol and ED consumers recruited from the general community (*M*=24, *SD*=3 years)

Table 1 Continued

Study	Study Design[a]	Method	Sample *N*[b]	Sample Characteristics
Ferreira et al. (2006)	Human experimental mixed ^	Double-blind placebo-controlled administration of: (i) alcohol (0.6g/kg or 1.0g/kg), (ii) 3.57mL/kg ED and (iii) alcohol and ED (peak mean BrAC 0.6g/kg: .050%; 1.0g/kg: .099%)	26	Healthy male moderate alcohol and ED consumers recruited from the general community (*M*=23.0, *SD*=3.0 years)
Marczinski et al. (2011)	Human experimental parallel #	Double-blind placebo-controlled administration of: (i) placebo, (ii) 0.65g/kg alcohol, (iii) 3.57mL/kg ED or (iv) AmED (peak mean BrAC .089%)	56	Healthy regular caffeine, alcohol, and ED consumers recruited from the university community (*n*=9 males; *M*=23.8, *SD*=3.4, range 21-33 years)
Marczinski et al. (2012)	Human experimental crossover ^	Double-blind placebo-controlled administration of: (i) placebo, (ii) 0.65g/kg alcohol, (iii) 3.57mL/kg ED or (iv) AmED (peak mean BrAC .071%)	18	Healthy regular caffeine, alcohol, and ED consumers recruited from the university community (*n*=9 males; *M*=22.9, *SD*=2.5, range 21-28 years)
Marczinski et al. (2013)	Human experimental parallel #	Double-blind placebo-controlled administration of: (i) placebo, (ii) 0.91mL/kg alcohol, (iii) 1.82mL/kg ED, or (iv) AmED (peak mean BrAC .043%)	80	Healthy regular male caffeine, alcohol, and ED consumers recruited from the university community (*n*=40 males; *M*=23.5, *SD*=3.1, range 21-33 years)
Peacock et al. (2013d)	Human experimental crossover ^	Single-blind placebo-controlled administration of: (i) placebo, (ii) 0.5g/kg alcohol, (iii) 1.82mL/kg ED, or (iv) AmED (peak mean BrAC .068%)	28	Healthy regular caffeine, alcohol, and ED consumers recruited from the general community (*n*=13 males; *M*=19.5, *SD*=1.8, range 18-25 years)

Note. [a] Note that ^ indicates within-subject comparisons for AmED-related analyses, whereas # indicates a between-subject design. [b] This number reflects the number of participants included in analyses; ALC=alcohol consumer sample size, AmED=AmED consumer sample size. ED: energy drink; AmED: alcohol mixed with energy drink; ns: not specified; * indicates that values were calculated from data supplied in the original manuscript.

2.6.5.2 Physiological Outcomes

Self-reported physiological outcomes of AmED versus alcohol consumption were assessed in three studies of consumers' real-life drinking experiences (de Haan et al., 2012; Peacock et al., 2012; Penning et al., 2011) and one study of consumers' expectations for drinking sessions (Woolsey et al., 2010) (Table 2). Varying assessment methodologies and tools were administered across these studies, including a 10-point severity scale (Penning et al., 2011), dichotomous (yes/no) response options (de Haan et al., 2012) or categories (outcome present/absent) (Peacock et al., 2012), and a 4-point agreement rating expectancy scale (Woolsey et al., 2010). Only two experimental laboratory studies were identified, one which assessed self-reported physiological state via 100-point visual analogue scale intensity ratings (Ferreira et al., 2006), while the other objectively assessed a limited range of physiological outcomes (Ferreira et al., 2004) (Table 2).

Studies assessing self-reported drinking experiences typically indicated significantly greater odds of musculoskeletal disturbance and cardiovascular elevations, and significantly lower odds of gastrointestinal upset, after AmED relative to alcohol. For example, Peacock et al. (2012) found that consumers reported higher odds of tremors and irregular heartbeat in AmED versus alcohol sessions. These consumers reported typical AmED intake of 2.4 standard 250mL EDs (~160mg caffeine). In contrast, Penning et al. (2011) reported equivalent odds of rapid heartbeat and nausea for AmED and alcohol consumers' ratings of their last hangover experience following consumption of the respective beverages. However, de Haan et al. (2012) and Peacock et al. (2012) reported significantly lower odds of nausea after AmED relative to alcohol consumption.

Table 2

Odds Ratio (OR) for Subjective Physiological Outcomes After AmED Relative to Alcohol Based on (i) Retrospective Self-Report of Drinking Experiences, and (ii) Current Report of Acute Dosing Effects in Laboratory Settings

	Between-Subject Self-Report of Drinking Experiences		**Within-Subject Self-Report of Drinking Experiences**						**Self-Report of Acute Dosing Experience (Laboratory Setting)**				**Objective Measurement of Acute Dosing Experience (Laboratory Setting)**			
Outcome	**Penning et al. (2011)[#a]**		**de Haan et al. (2012)^[a]**		**Peacock et al. (2012)^[a]**		**Woolsey et al. (2010)^[a]**		**Ferreira et al. (2006)^[b]**				**Ferreira et al. (2004)^[c]**			
	Last hangover[d]		**Last year[d]**		**Last six months[d]**		**Future AmED sessions[d]**		***30 minutes*[d]**		***120 minutes*[d]**		**15 minutes[d]**		**30 minutes[d]**	
	OR (95% CI)[e]	***p***	**OR (95% CI)[e]**	***p***	**OR (95% CI)[e]**	***p***	**OR (95% CI)[e]**	***p***	**OR (95% CI)[e]**	***p***	**OR (95% CI)[e]**	***p***	**OR (95% CI)[e]**	***p***	**OR (95% CI)[e]**	***p***
Musculoskeletal:																
Tension	-	-	-	-	-	-	-	-	1.50 (0.74, 3.05)	.257	0.75 (0.37, 1.50)	.412	-	-	-	-
Weakness	-	-	-	-	-	-	-	-	0.90 (0.50, 1.81)	.771	0.65 (0.32, 1.31)	.229	-	-	-	-
Tremors	-	-	-	-	2.48 (1.88, 3.27)	<.001	-	-	0.72 (0.35, 1.44)	.350	0.77 (0.38, 1.56)	.472	-	-	-	-
Cardiovascular:																
Irregular heartbeat			-	-	5.79 (3.84, 8.73)	<.001	-	-	-	-	-	-	-	-	-	-
Rapid heartbeat	0.58 (0.27, 1.21)	.148	-	-	-	-	7.09 (4.80, 10.48)	<.001	0.87 (0.43, 1.75)	.698	1.19 (0.59, 2.39)	.629	-	-	-	-
Gastrointestinal:																
Stomach ache	0.77 (0.37, 1.62)	.495	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Nausea~	0.85 (0.40, 1.78)	.663	0.03 (0.02, 0.05)	<.001	0.82 (0.68, 0.97)	.023	-	-	1.00 (0.50, 2.01)	1.00	0.87 (0.43, 1.74)	.685	-	-	-	-
Vomiting~	-	-	-	-	0.93 (0.74, 1.17)	.548	-	-	-	-	-	-	-	-	-	-

Table 2 Continued

Outcome	Between-Subject Self-Report of Drinking Experiences		Within-Subject Self-Report of Drinking Experiences						Self-Report of Acute Dosing Experience (Laboratory Setting)				Objective Measurement of Acute Dosing Experience (Laboratory Setting)			
	Penning et al. (2011) [#a]		de Haan et al. (2012)^[a]		Peacock et al. (2012)^[a]		Woolsey et al. (2010)^[a]		Ferreira et al. (2006)^[b]				Ferreira et al. (2004)^[c]			
	Last hangover[d]		Last year[d]		Last six months[d]		Future AmED sessions[d]		*30 minutes*[d]		*120 minutes*[d]		15 minutes[d]		30 minutes[d]	
	OR (95% CI)[e]	*p*	OR (95% CI)[e]	*p*	OR (95% CI)[e]	*P*	OR (95% CI)[e]	*p*	OR (95% CI)[e]	*p*	OR (95% CI)[e]	*p*	OR (95% CI)[e]	*p*	OR (95% CI)[e]	*p*
Disruption of Functioning:																
Alterations in hearing	-	-	-	-	1.17 (0.97, 1.41)	.108	-	-	1.00 (0.50, 2.01)	1.00	0.69 (0.34, 1.39)	.295	-	-	-	-
Alterations in vision	-	-	-	-	0.85 (0.73, 0.99)	.038	-	-	0.63 (0.31, 1.28)	.202	1.00 (0.50, 2.01)	1.00	-	-	-	-
Alterations in breathing	-	-	-	-	1.32 (0.90, 1.95)	.158	-	-	1.00 (0.50, 2.01)	1.00	1.00 (0.50, 2.01)	1.00	-	-	-	-
Alteration in walking	-	-	-	-	0.78 (0.68, 0.90)	.001	-	-	1.34 (0.66, 2.70)	.417	1.00 (0.50, 2.01)	1.00	-	-	-	-
Alteration in motor coordination	-	-	-	-	-	-	-	-	0.67 (0.33, 1.35)	.263	0.59 (0.29, 1.20)	.146	-	-	-	-
Alteration in speech	-	-	-	-	-	-	-	-	1.00 (0.50, 2.0)	1.00	1.00 (0.50, 2.01)	1.00	-	-	-	-
Increased speech	-	-	-	-	1.33 (1.11, 1.59)	.002	-	-	-	-	-	-	-	-	-	-
Speech slurred	-	-	-	-	0.68 (0.58, 0.80)	<.001	-	-	-	-	-	-	-	-	-	-
Inability to sleep or disrupted sleep	-	-	-	-	4.13 (3.08, 5.54)	<.001	4.13 (2.89, 5.88)	<.001	-	-	-	-	-	-	-	-
Reduced appetite	0.77 (0.37, 1.62)	.496	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Other CNS Disturbance:																
Dizziness	1.21 (0.58, 2.55)	.611	-	-	0.93 (0.81, 1.07)	.330	0.53 (0.38, 0.72)	<.001	0.90 (0.45, 1.80)	.756	0.69 (0.34, 1.40)	.305	-	-	-	-
Perspiration	-	-	-	-	1.15 (0.97, 1.37)	.107	-	-	0.61 (0.30, 1.25)	.176	1.12 (0.56, 2.24)	.758	-	-	-	-
Thirst	0.89 (0.42, 1.86)	.750	-	-	-	-	-	-	-	-	-	-	-	-	-	-

Table 2 Continued

Outcome	Between-Subject Self-Report of Drinking Experiences		Within-Subject Self-Report of Drinking Experiences						Self-Report of Acute Dosing Experience (Laboratory Setting)				Objective Measurement of Acute Dosing Experience (Laboratory Setting)			
	Penning et al. (2011) [#a]		de Haan et al. (2012)^[a]		Peacock et al. (2012)^[a]		Woolsey et al. (2010)^[a]		Ferreira et al. (2006)^[b]				Ferreira et al. (2004)^[c]			
	Last hangover[d]		Last year[d]		Last six months[d]		Future AmED sessions[d]		*30 minutes*[d]		*120 minutes*[d]		15 minutes[d]		30 minutes[d]	
	OR (95% CI)[e]	*p*	OR (95% CI)[e]	*p*	OR (95% CI)[e]	*p*	OR (95% CI)[e]	*p*	OR (95% CI)[e]	*p*	OR (95% CI)[e]	*p*	OR (95% CI)[e]	*p*	OR (95% CI)[e]	*p*
Other CNS Disturbance Continued:																
Salivation	-	-	-	-	1.13 (0.93, 1.39)	.225	-	-	1.19 (0.59, 2.39)	.631	2.68 (1.27, 5.65)	.010	-	-	-	-
Headache	0.94 (0.45, 1.98)	.873	-	-	0.94 (0.80, 1.10)	.414	-	-	0.74 (0.37, 1.50)	.403	0.81 (0.40, 1.63)	.551	-	-	-	-
Agitation	-	-	-	-	2.06 (1.54, 2.76)	<.001	-	-	1.78 (0.87, 3.65)	.112	1.10 (0.55, 2.21)	.789	-	-	-	-
'Jolt and crash episode'	-	-	-	-	1.64 (1.29, 2.08)	<.001	-	-	-	-	-	-	-	-	-	-
Overall wellbeing	-	-	-	-	-	-	-	-	1.29 (0.64, 2.59)	.482	-	-	-	-	-	-
Objective Outcomes:																
Blood pressure	-	-	-	-	-	-	-	-	-	-	-	-	0.60 (0.23, 1.58)	.298	0.16 (0.05, 0.52)	.002

Note. [a] Note that ^ indicates within-subject comparisons for AmED-related analyses, whereas # indicates between-subject comparison. The outcomes reported by Penning et al. (2011) reflect between-consumer ratings of AmED versus alcohol hangover experiences when they last consumed the respective beverages, whereas outcomes reported by de Haan et al. (2012) and Peacock et al. (2012) reflect within-consumer comparison of outcomes in the last year and last six months respectively in AmED versus alcohol drinking sessions; the former study involved dichotomous responses (yes/no) while in the latter study response options were grouped as outcome present ('half the time', 'most of the time', 'all of the time') or outcome absent ('none of the time', 'less than half the time'). Outcomes reported by Woolsey et al. (2010) also comprise within-consumer comparison, except AmED consumers were asked to report their expected behaviour in future AmED and alcohol drinking sessions, endorsing the likelihood of the outcome on a 4-point scale from 1 'disagree' to 4 'agree'. [b] The outcomes reported by Ferreira et al. (2006) reflect within-subject comparison of 100-mm visual-analogue change from baseline ratings after consuming 0.6g/kg or 1.0g/kg alcohol with or without 3.57mL/kg ED. [c] The outcomes reported by Ferreira et al. (2004) represent blood pressure (medium beats per minute) recorded using a semiautomatic sphygmomanometer after administration of 1.0g/kg alcohol with 3.57mL/kg ED. [d] Note that these times represent the time reference period for reporting (self-report of drinking experiences) or the minutes between beverage administration and subjective outcome administration (experimental research); note that those in italics only provided the time for commencing the test battery as a whole. [e] Odds ratios were calculated using the means and standard deviations or percentages/counts provided in-text, with the exception of those indicated by a ^, which were calculated using the means and *t*-statistic. An odds ratio of 1 indicates the event was equiprobable (or that the means were similar) for each consumer/in each session, > 1 indicates the event was more likely to occur (or that a higher mean was recorded) for AmED versus alcohol consumers/in AmED sessions relative to alcohol sessions, and <1 indicates the event is less likely to occur (or that a lower mean was recorded) for AmED versus alcohol consumers/in AmED sessions relative to alcohol sessions. ~Note that for the items 'nausea' and 'vomiting', de Haan et al. (2012) grouped the two outcomes as one item ('I have felt very sick to my stomach or thrown up after drinking'), whilst Peacock et al. (2012) limited assessed these two outcomes separately. A 'jolt and crash episode' refers to a sudden increase in energy followed by a sudden drop in energy. OR: odds ratio; 95% CI: 95% confidence interval.

In addition, participants in Peacock et al.'s (2012) study reported significantly lower odds of general functioning impairment, namely vision and walking, during AmED versus alcohol sessions, despite similar levels of alcohol consumption. However, in other aspects of functioning (e.g., sleep), participants reported increased odds of impairment (Peacock et al., 2012; Woolsey et al., 2010), or a shift in the type of impairment. For example, Peacock et al. (2012) found lower odds of slurred speech and higher odds of increased speech speed during AmED versus alcohol sessions.

Similar disturbances are evident when examining other central nervous system outcomes, with higher odds of agitation and 'jolt and crash episodes' in AmED sessions (Peacock et al., 2012). In contrast, retrospective studies assessing other physiological outcomes (e.g., dizziness, headache) had equivalent odds across session type or were inconsistent across studies. However, these studies may underestimate AmED outcomes: Penning et al. (2011) only asked consumers to reflect on experience in one drinking session, while Peacock et al. (2012) only identified the outcome as present in the last six months if participants responded 'half the time' or more often, excluding lower frequency occurrences.

In contrast with this research, the placebo-controlled double-blind experimental study assessing self-reported outcomes showed equivalent odds for musculoskeletal, cardiovascular, gastrointestinal, general functioning, and central nervous system disturbance ratings when consumers ingested alcohol (0.6g/kg or 1.0g/kg) with and without ED (3.57mL/kg), with the exception of increased salivation 120 minutes after AmED administration (Ferreira et al., 2006). The latter double-blind, placebo-controlled, crossover study (Ferreira et al., 2004) showed that blood pressure was

significantly decreased after administration of alcohol (1.0g/kg) with ED (3.57mL/kg) compared to alcohol without ED; consistent with caffeine's peak absorption time (30-60 minutes) (Benowitz, 1990), this effect was only evident at the later time point (30 minutes) (Ferreira et al., 2004).

2.6.5.3 Psychological Outcomes

Self-reported psychological outcomes of AmED versus alcohol were assessed in three studies of consumers' real-life drinking experiences (de Haan et al., 2012; Peacock et al., 2012; Penning et al., 2011) and one study of consumers' expectations for drinking sessions (Woolsey et al., 2010) (Table 3). Again, the number and type of outcomes assessed were not standardised across studies. These studies generally showed significantly higher odds of stimulation (Peacock et al., 2012), alertness (Peacock et al., 2012; Woolsey et al., 2010), and energy (Peacock et al., 2012), and significantly lower odds of fatigue (de Haan et al., 2012; Peacock et al., 2012), clumsiness (Woolsey et al., 2010), confusion (Peacock et al., 2012), and sadness (Peacock et al., 2012), during AmED relative to alcohol sessions. Penning et al. (2011) reported equivalent odds for 'tiredness' however, ratings were specific to the hangover experience.

This pattern of increased stimulation and decreased sedation has implications for the experience of other mood states. Peacock et al. (2012) found that consumers retrospectively self-reported higher odds of feeling irritable and 'on edge', and lower odds of feeling calm, carefree, friendly, outgoing, and sociable, during AmED relative to alcohol sessions. This psychological profile did not translate into more antisocial mood states, with equivalent odds of feeling annoyed or aggressive across

session type. Peacock et al. (2012) reported lower odds of feeling disinhibited during AmED sessions. However, other impulsive-type mood states (e.g., daring, adventuresome) showed equivalent odds across session type (Peacock et al., 2012; Woolsey et al., 2010).

In contrast to the physiological research, there was a greater body of experimental research available assessing psychological outcomes. Five double-blind placebo-controlled experimental studies were identified (Table 4); four of these studies (Marczinski et al., 2011; Marczinski et al., 2012, 2013; Peacock, Bruno, Martin, & Carr, 2013c) focused on assessing stimulation and sedation via a validated measure, the Biphasic Alcohol Effects Scale (Martin, Earleywine, Musty, Perrine, & Swift, 1993), whilst the other (Alford et al., 2001) adopted a more general measure of psychological state, the Profile of Mood States (McNair, Lorr, & Droppleman, 1979). The former four studies partially reflect real-life drinking experiences, in that participants generally reported significantly higher stimulation scores after ingesting alcohol (peak mean breath alcohol concentration (BrAC) .043% to 0.89%) with ED (1.82mL/kg to 3.57mL/kg) relative to alcohol alone (Marczinski et al., 2011; Marczinski et al., 2012, 2013; Peacock et al., 2013c). However, these studies did not typically identify AmED-induced reduced sedation, with equivalent odds for BAES sedation scores (Marczinski et al., 2011; Marczinski et al., 2012, 2013; Peacock et al., 2013c). Mental fatigue ratings were generally equivalent (Ferreira et al., 2006; Peacock et al., 2013c), with the exception of one study showing decreased ratings after AmED relative to alcohol (Marczinski et al., 2012).

Table 3

Odds Ratio (OR) for Subjective Psychological Outcomes after AmED Relative to Alcohol Based on Retrospective Self-Report of Drinking Experiences

Outcome	Between-Subject Self-Report of Drinking Experiences		Within-Subject Self-Report of Drinking Experiences					
	Penning et al. (2011)[#a]		de Haan et al. (2012)^[a]		Peacock et al. (2012)^[a]		Woolsey et al. (2010)^[a]	
	Last hangover[b]		Last year[b]		Last six months[b]		Future drinking session[b]	
	OR (95% CI)[c]	*p*	OR (95% CI)[c]	*p*	OR (95% CI)[c]	*P*	OR (95% CI)[c]	*p*
Stimulatory Mood:								
Stimulation	-	-	-	-	1.42 (1.22-1.66)	<.001	-	-
Alert/Clearheaded	-	-	-	-	2.34 (1.94-2.84)	<.001	5.98 (4.10, 8.73)	<.001
Energetic	-	-	-	-	1.79 (1.42-2.26)	<.001	-	-
Active	-	-	-	-	1.16 (0.99-1.35)	.071	-	-
Sedation Mood:								
Fatigued/Tired/Drowsy	0.81 (0.38, 1.70)	.569	0.25 (0.22, 0.28)	<.001	0.42 (0.34-0.54)	<.001	-	-
Clumsy	-	-	-	-	-	-	0.39 (0.28, 0.54)	<.001
Confused/ Mentally slow	-	-	-	-	0.68 (0.57, 0.80)	<.001	-	-
Sad	-	-	-	-	0.53 (0.38, 0.74)	<.001	-	-
Antisocial Mood:								
Feeling nervous/jittery/on edge	-	-	-	-	1.73 (1.33-2.24)	<.001	6.55 (4.46, 9.63)	<.001
Feeling annoyed	-	-	-	-	0.90 (0.73-1.12)	.336	-	
Feeling aggressive	-	-	-	-	1.22 (0.95-1.57)	.126	-	-
Feeling moody	-	-	-	-	-	-	1.10 (0.81, 1.50)	.556
Feeling irritable	-	-	-	-	1.30 (1.03-1.64)	.028	-	-

Table 3 Continued

Outcome	Between-Subject Self-Report of Drinking Experiences		Within-Subject Self-Report of Drinking Experiences					
	Penning et al. (2011)[#a]		de Haan et al. (2012)^[a]		Peacock et al. (2012)^[a]		Woolsey et al. (2010)^[a]	
	Last hangover[b]		Last year[b]		Last six months[b]		Future drinking session[b]	
	OR (95% CI)[c]	*p*	OR (95% CI)[c]	*p*	OR (95% CI)[c]	*P*	OR (95% CI)[c]	*p*
Novelty-Seeking Mood:								
Daring	-	-	-	-	1.01 (0.93. 1.01)	.796	0.79 (0.58, 1.08)	.145
Impulsive	-	-	-	-	0.92 (0.83, 1.01)	.087	-	-
Disinhibited/Boisterous	-	-	-	-	0.83 (0.75, 0.92)	.001	1.02 (0.75, 1.39)	.906
Adventuresome/Courageous	-	-	-	-	0.92 (0.81, 1.04)	.179	1.04 (0.77, 1.42)	.786
Positive Mood:								
Calm	-	-	-	-	0.50 (0.42, 0.59)	<.001	-	-
Carefree	-	-	-	-	0.73 (0.63, 0.84)	<.001	-	-
Friendly	-	-	-	-	0.58 (0.44, 0.78)	<.001	-	-
Outgoing	-	-	-	-	0.77 (0.63, 0.95)	.016	-	-
Sociable	-	-	-	-	0.67 (0.51, 0.88)	.004	-	-

Note. [a] Note that ^ indicates within-subject comparison for AmED-related analyses, whereas # indicates between-subject comparison. The outcomes reported by Penning et al. (2011) reflect between-consumer ratings of AmED versus alcohol hangover experiences when they last consumed the respective beverages, whereas outcomes reported by de Haan et al. (2012) and Peacock et al. (2012) reflect within-consumer comparison of outcomes in the last year and last six months respectively in AmED versus alcohol drinking sessions; the former study involved dichotomous responses (yes/no) while in the latter study response options were grouped as outcome present ('half the time', 'most of the time', 'all of the time') or outcome absent ('none of the time', 'less than half the time'). Outcomes reported by Woolsey et al. (2010) also comprise within-consumer comparison, except AmED consumers were asked to report their expected behaviour in future AmED and alcohol drinking sessions, endorsing the likelihood of the outcome on a 4-point scale from 1 'disagree' to 4 'agree'. [b] Note that these times represent the time reference period for reporting. [c] Odds ratios were calculated using the means and standard deviations or percentages/counts provided in-text, with the exception of those indicated by ^, which were calculated using the means and *t*-statistic. An odds ratio of 1 indicates the event was equiprobable (or that the means were similar) for each consumer/in each session, > 1 indicates the event was more likely to occur (or that a higher mean was recorded) for AmED versus alcohol consumers/in AmED sessions relative to alcohol sessions, and <1 indicates the event was less likely to occur (or that a lower mean was recorded) for AmED versus alcohol consumers/in AmED sessions relative to alcohol sessions. OR: odds ratio; 95% CI: 95% confidence interval.

Table 4

Odds Ratio (OR) for Subjective Psychological Outcomes after AmED Relative to Alcohol Based on Acute Dosing in Experimental Settings

Outcome	Alford et al. (2012)[#a]				Ferreira et al. (2006)^[a]				Marczinski et al. (2011)[#a]		Marczinski et al. (2012)^[a]		Marczinski et al. (2013)[#a]				Peacock et al. (2013c)^[a]			
	Drink 1: 45 minutes		*Drink 2: 45 minutes*		*30 minutes*		*120 minutes*		70 minutes		60 minutes		33 minutes		55 minutes		30 minutes		125 minutes	
	OR (95% CI)[c]	*p*	OR (95% CI)[c]	*p*	OR (95% CI)[c]	*P*	OR (95% CI)[c]	*p*	OR (95% CI)[c]	*p*	OR (95% CI)[c]	*p*	OR (95% CI)[c]	*p*	OR (95% CI)[c]	*p*	OR (95% CI)[c]	*p*	OR (95% CI)[c]	*p*
Stimulatory Mood:																				
Stimulation	-	-	-	-	-	-	-	-	2.60 (0.66, 10.18)	.171	2.53 (1.04, 6.16)*	.041	2.60 (0.83, 8.17)	.101	4.17 (1.30, 13.41)	.016	2.47 (1.18, 5.18)	.016	1.56 (0.77, 3.16)	.221
Alert/Clearheaded	0.16 (0.03, 0.85)	.032	0.04 (0.01, 0.24)	.001	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Energetic	0.63 (0.13, 3.10)	.567	0.01 (0.00, 0.11)	<.001	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Sedation Mood:																				
Sedation	-	-	-	-	-	-	-	-	#	#	0.61 (0.26, 1.43)	.256	0.81 (0.26, 2.48)	.707	0.91 (0.30, 2.81)	.874	1.50 (0.74, 3.04)	.261	0.82 (0.41, 1.65)	.575
Mental Fatigue/Drowsy	37.27 (5.33, 260.76)	<.001	269.16 (25.61, 2829.35)	<.001	0.82 (0.41, 1.64)	.567	0.91 (0.45, 1.83)	.794	#	#	0.31 (0.12, 0.78)*	.013	-	-	-	-	0.98 (0.49, 1.97)	.954	0.90 (0.45, 1.81)	.768
Clumsy	68.72 (8.75, 539.50)	<.001	9.09 (1.61, 51.33)	.012	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Confused/ Mentally slow	0.23 (0.04, 1.22)	.085	0.01 (0.00, 0.06)	<.001	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

Note. [a] ^ indicates within-subject comparison for AmED-related analyses, whereas # indicates between-subject comparison. The outcomes reported by: (i) Alford et al. (2012) reflect between-subject comparison of change from baseline ratings after drink 1 (.046% BrAC) and drink 2 (.087% BrAC) of alcohol with or without 250mL ED, (ii) Ferreira et al. (2006) reflect within-subject comparison of ratings at 30 minutes after consuming 0.6g/kg or 1.0g/kg alcohol with or without 3.57mL/kg ED, (iii) Marczinski et al. (2011) reflect between-subject comparison of change from baseline ratings after 0.65g/kg alcohol with or without 3.57mL/kg ED, (iv) Marczinski et al. (2012) reflect within-subject comparison of ratings after 0.65g/kg alcohol with or without 3.57mL/kg ED, (v) Marczinski et al. (2013) reflect between-subject comparison of ratings after 0.65g/kg alcohol with or without 3.57mL/kg ED, and (vi) Peacock et al. (2013c) reflect within-subject comparison of change from baseline ratings after consuming 0.50g/kg alcohol with or without 3.57mL/kg ED. All items were rated on 100-mm visual analogue scale (anchors: 0 'not at all' to 100 'very much') with the exception of: (i) stimulation and sedation, assessed using the Biphasic Alcohol Effects Scale (BAES), where subscale scores are derived following 11-point Likert ratings of 7 stimulant and 7 sedation adjectives, and (ii) outcomes reported by Alford et al. (2012), who used 100-mm visual analogue scales from the Profile of Mood States (McNair et al., 1979) representing bipolar adjective pairs of clearheaded-muzzy, clumsy-well-coordinated, energetic-lethargic, drowsy-alert, and mentally slow-quick witted. [b] Note that these times represent the minutes between beverage administration and subjective outcome administration; those in italics provided the time for commencing the test battery as a whole. [c] Odds ratios were calculated using the means and standard deviations or percentages/counts provided in-text, with the exception of those indicated by a ^, which were calculated using the means and *t*-statistic. An odds ratio of 1 indicates that the means were similar in the AmED and alcohol treatment conditions, > 1 indicates that a higher mean was recorded in the AmED relative to the alcohol condition, and <1 indicates that a lower mean was recorded in the AmED relative to the alcohol condition. # indicates that the data was not requested from the author. OR: odds ratio; 95% CI: 95% confidence interval; AmED: alcohol mixed with energy drink.

Table 5

Odds Ratio (OR) for Objective Cognitive and Motor Outcomes after AmED Relative to Alcohol Following Acute Dosing in Laboratory-Based Settings

Outcome	Alford et al. (2012)[a#]				Ferreira et al. (2006)[a^]								Marczinski et al. (2011)[a#]		Marczinski et al. (2012)[a^]	
	Drink 1: 45 minutes[b]		*Drink 2: 45 minutes*[b]		*30 minutes (0.6g/kg)*[b]		*30 minutes (1.0g/kg)*[b]		*120 minutes (0.6g/kg)*[b]		*120 minutes (1.0g/kg)*[b]		45 minutes[b]		45 minutes[b]	
	OR (95% CI)[c]	*p*	OR (95% CI)[c]	*p*	OR (95% CI)[c]	*p*	OR (95% CI)[c]	*p*	OR (95% CI)[c]	*p*	OR (95% CI)[c]	*p*	OR (95% CI)[c]	*p*	OR (95% CI)[c]	*p*
Reaction Time *Visual Reaction Time (CogReHab 95s) Cued Go/No-Go task (reaction time)*	-	-	-	-	2.33 (0.79, 6.85)	.126	1.00 (0.39, 2.59)	0.99	0.32 (0.10, 0.99)	.047	0.76 (0.29 (1.97)	.567	*Valid cue:* 0.16 (0.0, 0.67) *Invalid cue:* 0.35 (0.09, 1.39)	.012 .137	-	-
Flicker Discrimination *Critical Flicker Fusion Threshold*	0.18 (0.03, 0.96)	.045	8.54 (1.53, 47.87)	.015	-	-	-	-	-	-	-	-	-	-	-	-
Divided Attention: - Choice Reaction Time	1.67 (0.34, 8.25)	.529	0. 12 (0.02, 0.66)	.015	-	-	-	-	-	-	-	-	-	-	-	-
- Recognition Reaction Time	0.23 (0.04, 1.22)	.085	0.05 (0.01, 0.30)	.001	-	-	-	-	-	-	-	-	-	-	-	-
Immediate Memory *Immediate Memory Task*	828.11 (60.30, 11372.44)	<.001	0.39 (0.08, 1.97)	.255	-	-	-	-	-	-	-	-	-	-	-	-
Delayed Memory *Delayed Memory Task*	0.48 (0.10, 2.41)	.376	4.30 (0.82, 22.45)	.084	-	-	-	-	-	-	-	-	-	-	-	-
Inhibition *Stroop Cognitive Interference task (errors) Cued Go/No-Go task (inhibition failures)*	0.01 (0.00, 0.06)	<.001	0.00 (0.00, 0.05)	<.001	-	-	-	-	-	-	-	-	*Valid cue:* 0.32 (0.08, 1.26) *Invalid cue:* 1.00 (0.26, 3.83)	.102 .999	-	-

Table 5 Continued

Outcome	Alford et al. (2012)[a#]				Ferreira et al. (2006)[a^]								Marczinski et al. (2011)[a#]		Marczinski et al. (2012)[a^]	
	***Drink 1: 45 minutes*[b]**		***Drink 2: 45 minutes*[b]**		***30 minutes (0.6g/kg)*[b]**		***30 minutes (1.0g/kg)*[b]**		***120 minutes (0.6g/kg)*[b]**		***120 minutes (1.0g/kg)*[b]**		**45 minutes[b]**		**45 minutes[b]**	
	OR (95% CI)[c]	***p***	**OR (95% CI)[c]**	***p***	**OR (95% CI)[c]**	***p***	**OR (95% CI)[c]**	***p***	**OR (95% CI)[c]**	***p***	**OR (95% CI)[c]**	***p***	**OR (95% CI)[c]**	***p***	**OR (95% CI)[c]**	***p***
Information Processing																
Psychological Refractory Period Task	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.49 (0.20, 1.17)	.106
Visuo-Motor Control:																
- Fine motor control																
Grooved Pegboard Task	-	-	-	-	0.72 (0.26, 2.03)	.537	1.12 (0.43, 2.90)	.815	1.25 (0.45, 3.51)	.667	0.94 (0.36, 2.44)	.902	-	-	1.72 (0.73, 4.04)	.217
Purdue Pegboard Task:Assembly																
- Gross motor control																
Purdue Pegboard Task:Right Hand	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1.24 (0.54, 2.89)	.610

Note. [a] Note that ^ indicates within-subject comparison for AmED-related analyses, whereas # indicates between-subject comparison. The outcomes reported by: (i) Alford et al. (2012) reflect between-subject comparison of the change from baseline in performance outcomes on the a critical flicker fusion threshold task, choice reaction time task, word memory task, and Stroop cognitive interference task after drink 1 (.046% BrAC) and drink 2 (.087% BrAC) of alcohol with or without 250mL ED per alcohol dose, (ii) Ferreira et al. (2006) reflect within-subject comparison of outcomes on the CogReHab 95® and Grooved Pegboard test after consuming 0.6g/kg or 1.0g/kg alcohol with or without 3.57mL/kg ED, (iii) Marczinski et al. (2011) reflect between-subject comparison of the change from baseline in performance outcomes after 0.65g/kg alcohol with or without 3.57mL/kg ED after valid and invalid cued performance on a Cued Go/No-Go Task, and (iv) Marczinski et al. (2012) reflect within-subject comparison of outcomes on a Psychological Refractory Period task and Purdue Pegboard task after 0.65g/kg alcohol with or without 3.57mL/kg ED. [b] Note that these times represent the minutes between beverage administration and test administration; note that those in italics only provided the time for commencing the test battery as a whole. [c] Odds ratios were calculated using the means and standard deviations or percentages/counts provided in-text, with the exception of those indicated by a ^, which were calculated using the means and *t*-statistic. An odds ratio of 1 indicates the event was that the means were similar in the AmED and alcohol condition, > 1 indicates a higher mean was recorded in the AmED relative to alcohol condition, and <1 indicates that a lower mean was recorded in the AmED condition relative to alcohol condition. OR: odds ratio; 95% CI: 95% confidence interval; AmED: alcohol mixed with energy drink.

These experimental studies involved administration of a low ED dose, equivalent to one standard 250mL ED (80mg caffeine) per 70kg person. There has been one study using higher doses: Alford et al. (2012) administered participants two alcohol doses (peak BrAC .046% and .087%) across the session. Following a between-subjects design, placebo or active ED (one standard 250mL ED; 80mg caffeine) was co-administered with each alcohol dose. In contrast with previous findings, this study revealed significantly *lower* ratings of 'clearheaded' and 'energetic' after the first dose, and significantly *higher* subscale scores for 'mentally slow', 'clumsy', and 'drowsy' after both doses when ED was co-ingested. It should be noted that systematic between-subject variability in ratings for those in the active ED condition versus those in the placebo ED condition could contribute to these differences.

2.6.5.4 Cognitive and Motor Outcomes

To date, there has been little consistency in outcomes across cognitive studies; this may be due to the small number of measurements for each area of interest, the various tasks and doses adopted, and the different point during the blood alcohol concentration curve at which each have been assessed. For example, Alford et al. (2012) reported that AmED significantly decreased interference on the Stroop task, reflecting increased inhibitory control, whereas Marczinski et al. (2011) found equivalent rates of inhibition failures after valid and invalid cues on the Cued Go/No-Go task after AmED relative to alcohol. These discrepant methodological approaches make definitive conclusions regarding the relative cognitive effects of AmED challenging. In contrast, equivalence between AmED and alcohol administration has been consistently demonstrated across studies for motor

outcomes, with similar performance on fine and gross motor performance regardless of whether ED was co-ingested with alcohol or not.

2.6.5.5 Alcohol Intake and Priming

Seven studies were included that compared retrospective self-reported consumption patterns of AmED versus alcohol consumers (between-subject comparison) and four studies that compared AmED versus alcohol consumption patterns among AmED consumers (within-subject comparison) (Table 6). While these studies typically adopted similar indices of alcohol consumption with quantitative responses, the retrospective assessment period varied from 'tonight' to 'in the last year'. The authors of one paper declined the request for data (Thombs et al., 2010). Only one experimental study was identified in this area assessing motivation to drink following a priming dose; no studies were identified assessing ad libitum alcohol consumption following priming.

Studies undertaking between-subjects comparisons consistently indicate that AmED consumers report: (i) greater typical and maximum alcohol intake, (ii) more frequent alcohol use, and (ii) more frequent drunk/binge sessions. These results suggest that AmED consumers are riskier drinkers relative to alcohol consumers. Between-subjects field research assessing event level consumption and intoxication by AmED and alcohol consumers have revealed divergent outcomes: one study has shown a trend towards higher mean BrAC for AmED consumers (Rossheim & Thombs, 2011), whilst the other showed equivalent mean BrAC for the two consumer groups (Thombs et al., 2011).

Table 6

Odds Ratio (OR) For Self-Reported Intake and Frequency of Alcohol Use in Naturalistic Settings (i) by AmED versus Alcohol Consumers and (ii) in AmED versus Alcohol Drinking Sessions

Study	Reporting Time Period	Typical Intake		Maximum Intake		Use Frequency		Binge Use Frequency[a]		Drunk/Intoxicated Day Frequency[b]		Mean BrAC	
		OR (95% CI)[c]	*p*	OR (95% CI)[c]	*p*	OR (95% CI)[c]	*p*	OR (95% CI)[c]	*p*	OR (95% CI)[c]	*p*	OR (95% CI)[c]	*p*
						Between-Subject Comparison: Alcohol Quantity/Frequency for AmED versus Alcohol Consumer							
Brache and Stockwell (2011)	Last month	5.30 (3.49, 8.05)	<.001	5.58 (3.67, 8.49)	<.001	1.38 (0.92, 2.06)	.119	5.25 (3.46, 7.98)	<.001	3.61 (2.39, 5.46)^	<.001	-	-
de Haan et al. (2012)	Last month	2.80 (2.48, 3.16)	<.001	2.40 (2.13, 2.71)	<.001	1.45 (1.29, 1.64)	<.001	2.28 (2.03, 2.58)	<.001	2.13 (1.89, 2.41)	<.001	-	-
O'Brien et al. (2008)	Last month	1.44 (1.23, 1.68)	<.001	1.83 (1.57, 2.14)	<.001	-	-	2.06 (1.76, 2.40)	<.001	2.00 (1.71,2.34)^	<.001	-	-
Penning et al. (2011)	Last week	1.72 (0.82, 3.62)	.154	-	-	-	-	-	-	-	-	-	-
Rossheim and Thombs (2011)	Tonight	-	-	-	-	-	-	-	-	-	-	2.23 (0.93, 5.32)	.072
Thombs et al. (2011)	Tonight	-	-	-	-	-	-	-	-	-	-	1.85 (0.58, 5.88)	.297
Woolsey (2010); Woolsey et al. (2010)	Last year	3.56 (2.35, 5.38)*	<.001	6.14 (4.01, 9.40)*	<.001	3.45 (2.28, 5.21)*	<.001	4.33 (2.85, 6.57)	<.001	-	-	-	-

Table 6 Continued

Study	Reporting Time Period	Typical Intake		Maximum Intake		Use Frequency		Binge Use Frequency[a]		Drunk/Intoxicated Day Frequency[b]		Mean BrAC	
		OR (95% CI)[c]	***p***	**OR (95% CI)[c]**	***p***	**OR (95% CI)[c]**	***P***	**OR (95% CI)[c]**	***p***	**OR (95% CI)[c]**	***p***	**OR (95% CI)[c]**	***P***
		Within-Subject Comparison: Quantity/Frequency for AmED versus Alcohol Drinking Session											
Brache and Stockwell (2011)	Last month	1.72 (1.21, 2.46)*	.003	-	-	-	-	-	-	-	-	-	-
de Haan et al. (2012)	Last month	0.75 (0.69, 0.82)	<.001	0.17 (0.14, 0.20)	<.001	0.08 (0.07, .010)	<.001	0.19 (0.17, 0.21)	<.001	0.34 (0.31, 0.38)	<.001	-	-
Peacock et al. (2012, 2013a)	Last month (alcohol)/ Last 6 months (AmED)	1.26 (1.05, 1.51)*	.012	-	-	-	-	-	-	-	-	-	-
Price et al. (2010)	Last week	5.43 (1.41, 20.88)*	.014	-	-	-	-	-	-	-	-	-	-
Woolsey (2010); Woolsey et al. (2010)	Last year	0.42 (0.30, 0.58)	<.001	0.24 (0.17, 0.35)	<.001	0.16 (0.11, 0.24)	<.001	0.20 (0.14, 0.29)	<.001	-	-	-	-

Note. [a] Note that Brache and Stockwell (2011) and O'Brien et al. (2008) defined 'binge drinking' as four or more standard drinks for females and five or more standard drinks for males, de Haan et al. (2012) defined 'binge-drinking' as more than four/five standard drinks for females and males respectively, and Woolsey (2010) and Woolsey et al. (2010) defined 'binge-drinking' as consuming five or more standard drinks for males and females. [b] Those studies indicated with ^ asked participants reported the number of drunk days in a typical week. Note also that Brache and Stockwell (2011) asked participants to report the number of days 'intoxicated' while de Haan et al. (2012) and O'Brien et al. (2008) asked participants to report the number of 'drunk' days. [c] Odds ratios were calculated using the means and standard deviations or percentages/counts provided in-text, with the exception of those indicated by a *, which were calculated using the means and *t*-statistic. An odds ratio of 1 indicates the event is equiprobable (or that the means were similar) for each consumer/in each session, > 1 indicates the event was more likely to occur (or that a higher mean was recorded) for AmED versus alcohol consumers/in AmED sessions relative to alcohol sessions, and <1 indicates the event was less likely to occur (or that a lower mean was recorded) for AmED versus alcohol consumers/in AmED sessions relative to alcohol sessions. OR: odds ratio; 95% CI: 95% confidence interval; AmED: alcohol mixed with energy drink.

Within-subject comparison of alcohol consumption patterns are more mixed. Three studies (Brache & Stockwell, 2011; Peacock et al., 2012; Price et al., 2010) have shown significantly increased alcohol intake during AmED sessions relative to alcohol sessions, while two studies (de Haan et al., 2012; Woolsey et al., 2010) have shown the reverse. The former three studies defined AmED use as simultaneous use in one beverage (Peacock et al., 2012), simultaneous or premixed use (Brache & Stockwell, 2011) or ED use within one hour of alcohol consumption (Price et al., 2010), whereas the latter studies defined AmED use as ED consumption within two (de Haan et al., 2012) or four hours (Woolsey et al., 2010) of alcohol consumption. The latter studies have also shown significantly lower maximum alcohol intake, frequency of use, and binge/drunk session frequency during AmED sessions (de Haan et al., 2012; Woolsey et al., 2010).

The placebo-controlled between-subject double-blind experimental study (Marczinski et al., 2013) assessing motivation for alcohol intake following AmED and alcohol priming showed no significant difference in ratings of desire for more alcohol at 10 (OR=1.27, 95% CI[0.41,3.91], p=.679), 20 (OR=1.68, 95% CI[0.54,5.21], p=.366), 40 (OR=2.32, 95% CI[0.74,7.25], p=.147), 60 (OR=1.49, 95% CI[0.48,4.61], p=.485), or 80 (OR=1.57, 95% CI[0.51,4.84], p=.435) minutes. Baseline change scores were not calculated as ratings were compared across time within treatment condition. While no group differences were evident for baseline ratings (ps>.070), OR analyses may not account for differences between treatment groups which existed prior to administration.

2.6.6.6 Risk-Taking

One study was identified comparing retrospective self-reported behaviour by AmED versus alcohol consumers (Brache & Stockwell, 2011), two studies were identified comparing AmED versus alcohol consumers' engagement in alcohol-specific risk-taking (de Haan et al., 2012; O'Brien et al., 2008), and one study was identified comparing engagement in risk-taking by AmED and alcohol consumers after ingesting the respective beverage (Thombs et al., 2010); the request for data was declined for the final study (Table 7). These studies typically assessed select risk-taking behaviours relating to driving and sexual risk-taking, licit and illicit drug use, and physical harm, although items, and the retrospective reference period, were not standardised across studies. Only two within-subject studies were identified, both adopting subjective self-report measures (de Haan et al., 2012; Peacock et al., 2012), as well as one study examining risk-taking expectations (Woolsey et al., 2010) (Table 7). One experimental study was identified assessing the acute effects of AmED and alcohol on objective risk-taking (Peacock et al., 2013c). This dearth of within-subjects studies, particularly those circumventing self-report issues by adopting objective measures, limits inferences regarding the pharmacological impact of ED and alcohol co-ingestion on risk-taking.

Table 7

Odds Ratio (OR) for (i) Self-Reported Retrospective General Risk-Taking Behaviour by AmED versus Alcohol Consumers, (ii) Self-Reported Alcohol-Related Risk-Taking Behaviour by AmED versus Alcohol Consumers, and (iii) Self-Reported Retrospective Risk-Taking Behaviour by AmED Consumers during AmED versus Alcohol Drinking Sessions

Outcome	**Self-Reported General Risk-Taking Behaviour (Between-Subjects)[a]**		**Self-Reported Alcohol-Related Risk-Taking Behaviour (Between-Subjects)[b]**				**Self-Reported Risk-Taking Behaviour After AmED and Alcohol (Within-Subjects)[c]**					
	Brache and Stockwell (2011)#		**de Haan et al. (2012)#**		**O'Brien et al. (2008)#**		**de Haan et al. (2012)^**		**Peacock et al. (2012)^**		**Woolsey et al. (2010)^**	
	Last 12 months		**ns**		**Past 30 days**		**Last year**		**Last six months**		**Future drinking sessions**	
	OR (95% CI)[d]	***p***	**OR (95% CI)[d]**	***p***	**OR (95% CI)[d]**	***p***	**OR (95% CI)[d]**	***p***	**OR (95% CI)[d]**	***p***	**OR (95% CI)[d]**	***p***
General Risk-Taking:												
Took risks while drinking	2.48 (1.65, 3.72)	<.001	-	-	-	-	0.48 (0.42, 0.56)	<.001	-	-	1.07 (0.79, 1.46)	.655
Driving Risk-Taking:												
Drove motor vehicle after drinking	-	-	-	-	2.29 (1.88, 2.77)	<.001	0.55 (0.40, 0.76)	<.001	0.21 (0.13, 0.34)	<.001	1.38 (1.01, 1.89)	.043
Passenger while driver over legal alcohol limit	-	-	-	-	2.19 (1.83, 2.63)	<.001	-	-	0.24 (0.16, 0.36)	<.001	-	-
Seatbelt omission	-	-	-	-	-	-	-	-	0.38 (0.25, 0.57)	<.001	-	-
In vehicle with illegal passenger number	-	-	-	-	-	-	-	-	0.34 (0.26, 0.46)	<.001	-	-
In vehicle exceeding speed limit	-	-	-	-	-	-	-	-	0.58 (0.42, 0.81)	.001	-	-
Sexual Risk-Taking:												
Had sex with someone recently met	-	-	-	-	-	-	-	-	0.47 (0.38, 0.58)	<.001	-	-
Sex without contraception	-	-	-	-	-	-	-	-	0.51 (0.41, 0.62)	<.001	-	-
Was touched in unwanted sexual way	-	-	-	-	1.78 (1.22, 2.59)	.003	-	-	0.41 (0.29, 0.57)	<.001	-	-
Touched someone in unwanted sexual way	-	-	-	-	2.22 (1.34, 3.70)	.002	-	-	0.56 (0.36, 0.85)	.007	-	-
Got in sexual situation later regretted	-	-	-	-	-	-	0.41 (0.33, 0.51)	<.001	-	-	-	-

Table 7 Continued

Outcome	Self-Reported General Risk-Taking Behaviour (Between-Subjects)[a]		Self-Reported Alcohol-Related Risk-Taking Behaviour (Between-Subjects)[b]				Self-Reported Risk-Taking Behaviour After AmED and Alcohol (Within-Subjects)[c]					
	Brache and Stockwell (2011)#		de Haan et al. (2012)#		O'Brien et al. (2008)#		de Haan et al. (2012)^		Peacock et al. (2012)^		Woolsey et al. (2010)^	
	Last 12 months		ns		Past 30 days		Last year		Last six months		Future drinking sessions	
	OR (95% CI)[d]	*p*	OR (95% CI)[d]	*p*	OR (95% CI)[d]	*p*	OR (95% CI)[d]	*p*	OR (95% CI)[d]	*p*	OR (95% CI)[d]	*p*
Financial Risk-Taking:												
Spent more money than planned	-	-	-	-	-	-	-	-	0.47 (0.37, 0.60)	<.001	-	-
Gambled	-	-	-	-	-	-	-	-	0.34 (0.25, 0.46)	<.001	-	-
Aggressive and Antisocial Behaviour:												
Verbally fought~	-	-	-	-	-	-	0.62 (0.47, 0.83)	<.001	0.41 (0.33, 0.51)	<.001	-	-
Physically fought~	-	-	-	-	-	-	0.98 (0.73, 1.31)	.880	0.50 (0.38, 0.67)	<.001	1.06 (0.78, 1.44)	.724
Acted aggressively	-	-	-	-	-	-	-	-	-	-	1.68 (1.23, 2.31)	<.001
Asked to leave drinking establishment	-	-	-	-	-	-	-	-	0.45 (0.34, 0.60)	<.001	-	-
Vandalised	-	-	-	-	-	-	-	-	0.29 (0.13, 0.65)	.003	-	-
Cautioned/charged by the police	-	-	-	-	-	-	-	-	0.36 (0.17, 0.78)	.010	-	-
Acted on a dare which could cause harm	-	-	-	-	-	-	-	-	0.53 (0.40, 0.71)	<.001	-	-
Licit and Illicit Drug Use:												
Smoked cigarettes	-	-	2.37 (2.06, 2.72)	<.001	-	-	-	-	0.59 (0.51, 0.69)	<.001	-	-
Drank more alcohol than planned	-	-	-	-	-	-	-	-	0.54 (0.43, 0.68)	<.001	-	-
Used legal drugs~	-	-	0.99 (0.85, 1.16)	.887	-	-	-	-	0.56 (0.44, 0.71)	<.001	-	-
Used illegal drugs~	3.27 (1.76, 6.09)	<.001	2.20 (1.91, 2.54)	<.001	-	-	-	-	0.42 (0.33, 0.53)	<.001	-	-

Table 7 Continued

Outcome	Self-Reported General Risk-Taking Behaviour (Between-Subjects)[a]		Self-Reported Alcohol-Related Risk-Taking Behaviour (Between-Subjects)[b]				Self-Reported Risk-Taking Behaviour After AmED and Alcohol (Within-Subjects)[c]					
	Brache and Stockwell (2011)#		de Haan et al. (2012)#		O'Brien et al. (2008)#		de Haan et al. (2012)^		Peacock et al. (2012)^		Woolsey et al. (2010)^	
	Last 12 months		ns		Past 30 days		Last year		Last six months		Future drinking sessions	
	OR (95% CI)[d]	*p*	OR (95% CI)[d]	*p*	OR (95% CI)[d]	*p*	OR (95% CI)[d]	*p*	OR (95% CI)[d]	*p*	OR (95% CI)[d]	*p*
Physical Harm:												
Passed out	-	-	-	-	-	-	1.24 (0.82, 1.88)	0.299	0.47 (0.38, 0.59)	<.001	-	-
Physically hurt or injured~	-	-	-	-	2.24 (1.68, 2.98)	<.001	0.52 (0.41, 0.65)	<.001	0.46 (0.36, 0.58)	<.001	1.17 (0.86, 1.60)	.325
Required medical treatment	-	-	-	-	2.20 (1.20, 4.02)	.011	-	-	0.24 (0.08, 0.73)	.012	-	-
Psychological Distress:												
Behaved in a way which resulted in later guilt/regret~	-	-	-	-	-	-	0.47 (0.39, 0.56)	<.001	0.36 (0.30, 0.44)	<.001	-	-
Behaved in a way which resulted in later humiliation/embarrassment	-	-	-	-	-	-	0.03 (0.02, 0.05)	<.001	0.50 (0.42, 0.60)	<.001	-	-

Note. [a] Note that ^ indicates within-subject comparison for AmED-related analyses, whereas # indicates between-subject comparison. The outcomes reported by Brache and Stockwell (2011) reflect between-subject comparison of general behaviour in the last 12 months for AmED versus alcohol consumers. [b] The outcomes reported by de Haan et al. (2012) reflect between-subject comparison of alcohol-related behaviour in the last 12 months for AmED versus alcohol consumers, (ii) O'Brien et al. (2008) reflect between-subject comparison of alcohol-related consequences in the last 30 days for AmED versus alcohol consumers, and (iii) Thombs et al. (2010) reflect between-subject comparison of prospective behaviour for AmED and alcohol consumers whilst under the influence of the respective beverages. [c] The outcomes reported by: (i) de Haan et al. (2012) and Peacock et al. (2012) reflect within-subject comparison of outcomes in the last year and last six months respectively in AmED versus alcohol drinking sessions, with both studies comprising dichotomous responses (yes/no), and (ii) Woolsey et al. (2010) reflect within-subject comparison of prospective expectations of outcomes in AmED and alcohol drinking sessions, endorsing the likelihood of the outcome on a 4-point Likert scale from 1 'disagree' to 4 'agree'. [d] Odds ratios were calculated using the means and standard deviations or percentages/counts provided in-text, with the exception of those indicated by a *, which were calculated using the means and *t*-statistic. An odds ratio of 1 indicates the event was equiprobable for each consumer/in each session, > 1 indicates the event was more likely to occur for AmED versus alcohol consumers/in AmED sessions relative to alcohol sessions, and <1 indicates the event was less likely to occur for AmED versus alcohol consumers/in AmED sessions relative to alcohol sessions. ~ For the item 'verbally fought' de Haan et al. (2012) specified that this comprised being 'very rude, obnoxious or insulting'. For the item 'more likely to fight' Peacock et al. (2012) specified that this referred only to physical fighting, while Woolsey et al. (2010) and de Haan et al. (2012) did not specify whether 'fighting' referred to physical or verbal interaction. For the item 'used legal drugs' Peacock et al. (2012) specified that this referred only to recreational use, whereas de Haan et al. (2012) referred to medication use in general. For the item 'used illegal drugs' Brache and Stockwell (2011) specified that this referred only to stimulant drugs, while de Haan et al. (2012) referred to drug use in general. For the item 'physically hurt or injured' Peacock et al. (2012) limited this to harm specific to the consumer, while de Haan et al. (2012) specified that the physical hurt or harm could be to the consumer or others around them. For the item 'behaved in a way which resulted in me later experiencing guilt or regret', de Haan et al. (2012) worded this item as 'while drinking, I have said or done embarrassing things'. OR: odds ratio; 95% CI: 95% confidence interval; AmED: alcohol mixed with energy drink; ns: not specified.

The studies undertaking between-subject comparison of general risk-taking showed increased odds of general risk-taking and tobacco and illicit drug use (Brache & Stockwell, 2011). Similarly, the studies comparing engagement in alcohol-specific risk-taking, showed that AmED consumers reported significantly increased odds of taking and having been taken advantage of sexually, being physically hurt or injured, requiring medical treatment, being a passenger in a car with a driver over the legal alcohol limit and driving whilst under the influence (de Haan et al., 2012; O'Brien et al., 2008).

The results of the within-consumer retrospective comparison studies directly contrast with these outcomes (de Haan et al., 2012; Peacock et al., 2012). In these studies, participants reported consistently lower odds of risk-taking in AmED sessions across a range of behaviours, including driving, sexual risk-taking, financial risk-taking, aggressive and anti-social behaviour, licit and illicit drug use, and physical harm/injury and psychological distress. Only two outcomes were discrepant: de Haan et al. (2012) reported equivalent odds of 'being in a physical fight' and 'passing out', whilst Peacock et al. (2012) reported lower odds of aggressive and antisocial behaviour in AmED sessions.

In contrast, the experimental within-subject objective comparison of risk-taking has revealed divergent results compared to retrospective self-report (Peacock et al., 2013c). The experimental study involved administration of the Balloon Analogue Risk Task (Lejuez et al., 2002), where participants are reimbursed for each pump of a simulated balloon if they discontinue prior to the predetermined explosion point. If the balloon explodes, the money is forfeited. This study revealed equivalent odds of

risk-taking, as indexed by the adjusted number of pumps (OR=1.43, 95%CI[0.73, 2.82], *p*=.301), total earnings (OR=0.79, 95%CI[0.40, 1.55], *p*=.494), and total number of explosions (OR=1.65, 95%CI[0.83, 3.28], *p*=.149), after administration of alcohol (mean peak BrAC .068%) with and without ED (3.57mL/kg). However, it should be noted that there was no effect of alcohol on task performance, suggesting low task sensitivity to interactive effects.

2.6.6 Discussion

2.6.6.1 Available Evidence

Overall, the body of literature on AmED is typically dominated by retrospective self-report studies. With the exception of the alcohol intake research, the types of items assessed, item wording, and response type generally differ across studies. Furthermore, in some areas there is a predominance of between-subject research, meaning that individual differences between consumer groups confound conclusions regarding the effect of AmED. Few experimental studies were identified, particularly in regards to studies adopting objective measures. The reliance on self-reported drinking experience data, particularly retrospective data, introduces other potential contributing psychological (e.g., expectancy), individual (e.g., trait personality), and environmental (e.g., drinking environment) factors which could influence outcomes, as well as methodological concerns (e.g., recall bias). Despite the increase in AmED research over the past few years (68% of the reviewed articles were published between 2011 and 2013), the general lack of research in this area is surprising considering the public attention dedicated to this consumption trend and current endeavours to determine an appropriate policy response.

2.6.6.2 General Overview

2.6.6.2.1 Physiological Outcomes

The preliminary evidence from research assessing self-reported outcomes of AmED consumption indicates potential changes to the nature of intoxication, with consumers more likely to experience musculoskeletal (e.g., tremors), cardiovascular (e.g., increased heart rate), and general central nervous system (e.g., agitation) disturbance. It is theorised that these outcomes may be a consequence of the stimulatory effects of EDs, consistent with the common side-effects of caffeine overconsumption (Gunja & Brown, 2012). Consumers also report reduced sedation-based outcomes, specifically: nausea, walking difficulty, and vision difficulties, although the few instances of measurement for these outcomes should be emphasised. The dual effect of ED co-ingestion is illustrated most clearly when examining transient speech impairment, with consumers reporting increased odds of faster speech, and lower odds of slurred speech, in AmED sessions in one study. Several primary intoxication outcomes (e.g., dizziness, headache) showed equivalent odds in AmED and alcohol sessions.

2.6.6.2.2 Psychological Outcomes

The profile of increased stimulation and decreased sedation during AmED consumption is generally mirrored in self-reported real-life psychological outcomes. The experimental literature is more contrary. Participants have reported enhanced stimulation after laboratory-based AmED administration. In contrast, ratings of sedation typically do not differ between AmED and alcohol treatment conditions. These effects are typically recorded at low ED doses (one standard 250mL ED per

70kg person). However, potential dose-dependent effects of AmED were identified, in that the only study which administered a moderate ED dose (two standard 250mL EDs administered approximately one hour apart) revealed decreased stimulation-related psychological outcomes and increased sedation-related psychological outcomes after AmED administration (Alford et al., 2012). However, as acknowledged by the authors, the outcomes may be a function of the methodology. No studies were identified which systematically assessed the dose-dependent effects of ED with a set alcohol dose.

2.6.6.2.3 Cognitive and Psychomotor Outcomes

As noted in the results section, the lack of standardisation in the aspects of cognitive and motor performance assessed and the methodological characteristics (i.e., test measures and doses administered, time of testing) of the few studies conducted undermines definitive conclusions regarding the relative cognitive effects of AmED and alcohol. While the literature consistently indicates that ED co-ingestion does not alter motor outcomes, the studies overviewed had only involved administration of a single low ED dose. Consequently, there is no solid evidence base regarding the dose-dependent effects of AmED. Furthermore, different measures have been adopted across studies, making generalised conclusions regarding the interactive effect of AmED on cognitive and motor outcomes difficult.

2.6.6.2.4 Hazardous Drinking

AmED physiological and psychological outcomes are theorised to increase the likelihood of excess alcohol intake and risk-taking behaviour by decreasing sedation-based cues of intoxication (Ferreira et al., 2006; Marczinski et al., 2011), creating a

state of 'wide-awake drunkenness' (Arria & O'Brien, 2011). This review indicated that AmED consumers consistently report more risky drinking practices than alcohol consumers. However, the few studies comparing alcohol intake in AmED versus alcohol sessions have provided mixed support for this hypothesis, with several studies revealing *increased* intake (Brache & Stockwell, 2011; Peacock et al., 2012; Price et al., 2010), whilst others indicate *decreased* intake (de Haan et al., 2012; Woolsey et al., 2010), in AmED relative to alcohol sessions. Attempts to reconcile these results point predominantly to the lack of standardisation in defining AmED, however it is important to note that all but one (Peacock et al., 2012) of these studies focused only on college student consumers, a subgroup who typically display high-risk drinking practices (Ham & Hope, 2003). Comparison of alcohol intake following an acute AmED and alcohol priming dosing in a controlled setting could control for external influences. However, no experimental studies examining ad-libitum alcohol consumption following an AmED or alcohol priming dose were identified. The only experimental study to indirectly assess the effects of AmED on alcohol consumption, via ratings of motivation to drink, showed equivalent outcomes. Consequently, the hypothesis that AmED consumption increases subsequent alcohol intake cannot be discounted due to the equivocal nature of the literature.

2.6.6.2.5 Risk-Taking

AmED consumers report greater risk-taking behaviour relative to alcohol consumers. However, two studies have shown that AmED consumers consistently self-report less risk-taking in AmED versus alcohol sessions (de Haan et al., 2012; Peacock et al., 2012) and one study showed lower odds of self-reported feelings of disinhibition

in AmED sessions (Peacock et al., 2012). These results contradict common assumptions regarding the behavioural effects of AmED (Weldy, 2010). One explanation may be that AmED-induced increases in alertness may improve consumers' attentional capacity for decision-making (Peacock et al., 2012). However, these preliminary studies may underestimate risk-taking in AmED sessions. Analyses did not account for the relative frequency of AmED and alcohol sessions (Peacock, Bruno, & Martin, 2013b; Rossheim, Suzuki, & Thombs, 2013). Only one experimental study was identified as assessing state-dependent changes in behavioural risk-taking, contradicting common assumptions regarding the behavioural effects of AmED and revealing equivalent odds of risk-taking after AmED and alcohol (Peacock et al., 2013c). These outcomes may potentially be a consequence of low task sensitivity to the doses administered. No studies were identified assessing the dose-dependent effects of AmED on risk-taking to determine whether interactive AmED effects on risk-taking become apparent at doses similar to those ingested in real-life drinking contexts.

2.6.6.3 Limitations

Conclusions based on this review are limited, in that there is no data currently available as to the relative clinical severity and dose threshold at which physiological and psychological changes of AmED occur. While there are guidelines outlining the recommended maximum daily ED intake to minimise adverse outcomes (Food Standards Australia and New Zealand, 2001), laboratory-based research controlling for external confounds has generally shown no difference in physiological, psychological, cognitive, psychomotor, and behavioural outcomes following AmED and alcohol administration. However, these studies have generally investigated the

effect of ED co-ingestion at a dose lower than that typically ingested in real-life settings, restricting ecological validity and generalizability.

Secondly, these conclusions are primarily based on consumers' retrospective reflection on a number of drinking sessions over an extended time period, with potentially variable intake in each session and possible concomitant use of other licit and illicit substances. It is premature to attribute these outcomes solely to the pharmacological effects of co-ingestion. Discrepancies between retrospective and prospective reports suggest that AmED consumers may have specific expectations regarding AmED intoxication which may not be evidence-based. It has been well-established that consumer expectancies regarding the interactive effects of caffeine and alcohol can alter performance independent of actual administration (Fillmore et al., 2002); whether these results translate to AmED consumers' intoxication experience remains unexplored.

While laboratory-based assessment can reduce ecological validity, the controlled environment and beverage blinding can reduce the impact of these confounding variables. Outcomes can be objectively assessed to eliminate potential self-report biases and a within-subject design s for systematic individual differences. Acute dosing protocols can link specific doses with changed outcomes. As aforementioned, this review revealed no experimental research assessing high ED doses or the dose-dependency of ED effects when co-ingested with a set alcohol dose. As such, we cannot determine whether the self-reported outcomes are an accurate reflection of the pharmacological effects of AmED or a product of intertwined environmental (e.g., drinking environment), psychological (e.g., expectancy effects), and

methodological (e.g., recall bias) factors. Furthermore, the majority of the outcomes considered in this review have only been assessed in one or two studies. The lack of research assessing the pharmacological effects of AmED to determine the clinical severity of, and dose threshold for, negative physiological and psychological outcomes means that there is no solid evidence-base to inform public health policy at present.

Similar issues are evident when characterising the causal link between AmED consumption and likelihood of excess alcohol intake and risk-taking behaviour. The general lack of research (particularly experimental research) coupled with inconsistent outcomes between studies impedes the construction of a strong evidence-base to determine whether AmED offers additional behavioural harms relative to alcohol. However, this review consistently indicated that AmED consumers comprise a subgroup with a higher predisposition towards risky behaviour. Potential state-dependent changes in behavioural outcomes, coupled with a trait tendency towards risky behaviour, could place this consumer group at higher risk of experiencing or causing harm. Harm reduction policies should be targeted at this group to ensure that consumers are educated regarding the potential side-effects of AmED.

2.6.6.4 Conclusions

In sum, this review indicated that AmED consumption may exert a dual effect, increasing stimulation-based outcomes and reducing specific sedation-based physiological outcomes relative to when alcohol is consumed without ED. However, the literature is mixed as to whether these changes in the nature of intoxication

translate into an increased likelihood of greater alcohol intake and risk-taking behaviour. Despite the growth in AmED popularity, there is a paucity of research assessing the relative pharmacological effects of alcohol ingested with and without ED at naturalistic consumption levels. As such, it is imperative that further research is undertaken to determine the clinical severity and dose threshold at which AmED-induced changes in the physiological, psychological, and behavioural nature of intoxication occur.

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2.6.9 Consequences of Using Alcohol Mixed with Energy Drinks: Summary

The systematic review highlights that there is a very small number of studies directly assessing the effects of AmED by comparing self-reported outcomes following AmED versus alcohol consumption within the same individuals. It is particularly pertinent that future research extends beyond university student drinking culture to encompass the drinking experiences of AmED consumers in the general community. Furthermore, the review emphasises the need for experimental research directly assessing the self-reported and objective pharmacological effects of set alcohol and ED doses in controlled settings. Such research is required to minimise confounding variables (e.g., drinking environment) and determine the intake threshold at which changes are observed.

As noted in the Preface (Section 2.6.1), this review incorporated publications within this thesis which relating specifically to physiological, psychological, and behavioural risk-taking consequences of AmED use (Chapters 3, 4, and 6). Bearing this in mind, the primary research questions which arise from this chapter (and which formed the basis for these publications) are:

- Are there any appreciable differences in the physiological, psychological, and behavioural outcomes of AmED versus alcohol consumption when comparing retrospective self-reported drinking experiences for the same individual?
- Are any changes in self-reported physiological and psychological side-effects after AmED relative to alcohol evident when comparing the effects of an acute dose of AmED and alcohol in a controlled environment for the same individual?

- Are any changes in objectively assessed risk-taking behaviour evident when comparing the effects of an acute dose of AmED and alcohol in a controlled environment for the same individual?

2.7 Impulsive Behavioural Consequences of Using Alcohol Mixed with Energy Drinks

2.7.1 Overview

As noted in the systematic review, comparison of AmED versus alcohol consumers typically shows greater risk-taking by the former. The few studies comparing within-subject retrospective self-reported risk-taking behaviour after consumption of AmED compared to alcohol have revealed mixed results, with some studies showing that consumers report greater alcohol intake in AmED sessions (L. Berger et al., 2011; Price et al., 2010), whilst others show lesser alcohol intake in AmED sessions (de Haan et al., 2012; Woolsey et al., 2010) and decreased odds of risk-taking (de Haan et al., 2012). Consequently, changes in risk-taking behaviour following AmED consumption may be an interaction between: (i) trait characteristics of individuals attracted to AmED consumption, and (ii) state-dependent behavioural changes as a consequence of AmED consumption.

Risk-taking and behavioural impulsivity are distinct, but related, processes. Changes in impulsive behaviour may impact on the likelihood of risk-taking, in that an impaired ability to wait for and process information or to evaluate consequences could increase the likelihood of engaging in risky behaviours. Impulsivity can be broadly defined as a tendency to engage in inappropriate or maladaptive behaviours (de Wit, 2009). Self-report measures are typically administered to assess trait impulsivity. State-dependent changes in impulsivity are typically assessed using laboratory-based measures, as they can provide a sensitive and objective indication of transient changes in behaviour (Dougherty, Mathias, Marsh, & Jagar, 2005). While self-report measures of trait impulsivity generally correlate highly with one

another, there is typically a weak correlation between self-report and laboratory impulsivity measures (Lane, Cherek, Rhoades, Pietras, & Tcheremissine, 2003), indicating that the latter may explain unique aspects of impulsivity not assessed by self-report measures (Dougherty et al., 2005).

Impulsivity can be both an antecedent and consequence of alcohol consumption (de Wit, 2009). As an antecedent to alcohol use, trait impulsivity has been associated with alcohol use initiation, continuation, and abuse (Lejuez et al., 2010). As a consequence of alcohol use, increases in impulsive behaviour have been observed in laboratory-based assessment following acute alcohol administration (Marczinski & Fillmore, 2005b). Research has yielded differential effects of alcohol on validated laboratory-based quantitative measures of behavioural impulsivity, suggesting that there are several measurably different underlying processes associated with impulsive behaviour (de Wit, 2009; Dick, 2010)

The number of processes underlying impulsivity has been the subject of debate (Dougherty et al., 2005; Evenden, 1999; Lejuez et al., 2010; Reynolds, Penfold, & Patak, 2008), with as few as two (Reynolds et al., 2008) and as many as five (Meda et al., 2009) factors proposed. Impulsivity can be apparent across several stages of information processing: response preparation, response execution, and consequence assessment (Evenden, 1999). Previous research assessing behavioural impulsivity has typically focussed on the latter two stages. Impulsivity at the response execution stage is motor-based, whereby individuals can show: (i) a tendency to respond before stimulus processing and evaluation is complete (impulsive response initiation) and (ii) a reduced ability to suppress responses that are inappropriate in the specific

context (response disinhibition). Impulsivity at the consequence assessment stage is cognitive-based, whereby individuals show reward-focused responding with a preference for more immediate, smaller rewards compared to delayed larger rewards (impulsive decision-making*)* (de Wit, 2009; Lane et al., 2003; Reynolds et al., 2008)[16].

Research assessing the effects of alcohol on impulsive response execution, response disinhibition, and impulsive decision-making will be overviewed in the following section. This discussion will incorporate studies examining the effects of caffeine and ED, alone and in combination with alcohol, on these facets of impulsivity, in order to determine the current state of the literature regarding the potential impact of AmED consumption on behavioural impulsivity.

2.7.2 Impulsive Response Initiation

2.7.2.1 Measurement of Impulsive Response Initiation

Impulsive response initiation has commonly been measured using a Continuous Performance Test (CPT) paradigm (Beck, Bransome, Mirsky, Rosvold, & Sarason, 1956), whereby participants make selective responses to a target stimuli (e.g., the single letter A; *single-stimuli task*), or a stimulus which is preceded by another stimulus (e.g., A followed by B; *paired-stimuli sequence task*); incorrect responses to stimuli other than the target, otherwise known as commission errors, are thought

[16] Behavioural impulsivity evident at the first stage of processing is also cognitive-based. This type of impulsivity is known as 'reflection impulsivity', whereby individuals have a tendency to make decisions under conditions of uncertainty, before they have obtained all the necessary information (Clark, Robbins, Ersche, & Sahakian, 2006; Kagan, 1965). This doctoral research will focus only on the aspects of behavioural impulsivity occurring in the second and third stage of processing.

to index impulsive response initiation. The Immediate Memory/Delayed Memory Task (IMT/DMT; Dougherty, Marsh, & Mathias, 2002) was developed as an extension of the CPT paradigm due to ceiling effects from insufficient task difficulty (Cornblatt & Keilp, 1994). In the IMT/DMT, participants respond selectively to a 5-digit target stimulus when it matches the preceding stimulus (e.g., '34589' followed by '34589'). The IMT/DMT offers a more complex assessment than traditional CPT tasks, including two types of non-targets ('catch' stimuli which differ from the target by one digit and 'non-target' stimuli which are random) and an additional level of task difficulty by introducing a delayed memory component. In the delayed memory component, distractor stimuli are repeatedly presented in the interval between paired stimuli. The IMT/DMT also adopts a more restrictive measure of impulsive inattention, focusing only on commission errors to similar non-targets, as these errors are theorised to result from an inability to withhold a response until stimulus processing is completed. This index of impulsivity has been validated in past research with high trait impulsivity samples, including those diagnosed with alcohol dependence (Bjork, Hommer, Grant, & Danube, 2004), bipolar disorder (Swann, Anderson, Dougherty, & Moeller, 2001) and disruptive behaviour disorders (Dougherty et al., 2003; Dougherty, Bjork, Marsh, & Moeller, 2000a).

2.7.2.2 Alcohol and Impulsive Response Initiation

Only four studies have been conducted to date looking at the effects of alcohol on IMT/DMT performance (Dougherty et al., 2008; Dougherty, Marsh, Moeller, Chokshi, & Rosen, 2000b; Dougherty et al., 1999; S. C. Reed et al., 2012). These studies revealed a dose-dependent effect of alcohol on IMT performance, with no statistically significant change in impulsive response initiation detected when low

alcohol doses were administered (mean peak BrAC .011% to .056%) but increased impulsive responding when high alcohol doses (mean peak BrAC .063% to .092%) were administered (Dougherty et al., 2008; Dougherty et al., 2000b; Dougherty et al., 1999; S. C. Reed et al., 2012). Closer examination of these studies also showed that detection of alcohol-induced increases in impulsive response initiation was dependent on the specific index adopted. The ratio of commission errors to correct detections was identified as the most sensitive outcome indicative of impulsive response initiation (relative to the frequency of commission errors), accounting for systematic individual variation in discriminability (Dougherty et al., 2000b).

The results are more mixed when looking at impulsive response initiation under greater task difficulty, as indexed by the DMT. Dougherty et al. (1999) reported that ingestion of a low alcohol dose (peak mean BrAC .035%) increased commission error rate, and S. C. Reed et al. (2012) found that a moderate (mean peak BrAC .056%) and high (mean peak BrAC .092%) alcohol dose increased the ratio of commission errors to correct detections, relative to placebo administration. In contrast, Dougherty et al. (2000b) reported no effect of a low (mean peak BrAC .039%) or high (mean peak BrAC .091%) alcohol dose on commission error rate or ratio of commission errors to correct detections. The researchers theorise that the DMT may be less robust in detecting the effects of alcohol than the IMT, as it has fewer trials per block, increasing the variability of outcomes.

2.7.2.3 ED, Alcohol, and Impulsive Response Initiation

Overall, these studies suggest that alcohol administration increases impulsive response initiation in a dose-dependent manner, particularly when task difficulty is

lower, with impairment typically evident following moderate doses (BrAC ≥ .063%). However, there have been no studies assessing whether ED co-ingestion increases, attenuates, or maintains alcohol-induced impairment of impulsive response initiation. In fact, there is a lack of research in this field investigating the effect of caffeine or ED in general, regardless of alcohol co-ingestion. Those few studies which have assessed impulsive response initiation following caffeine or ED administration have typically revealed no statistically significant effect of either substance. For example, Bernstein et al. (1994) found that children's commission error rates on a single-stimuli CPT were not impacted by administration of caffeine (2.5mg/kg and 5.0mg/kg). Similarly, administration of 200mg caffeine or a standard 250ml ED has been shown to have no statistically significant impact on single-stimuli CPT commission error rates relative to placebo administration (Gendle et al., 2009). A commonality across these studies is the use of a single-stimuli CPT paradigm, meaning that the absence of treatment effects may be a consequence of low task sensitivity. Thus, it cannot be inferred from this research whether ED consumption does have an effect on impulsive response initiation, independently or in combination with alcohol.

2.7.3 Response Disinhibition

2.7.3.1 Measurement of Response Disinhibition

This process is based on the theory of cognitive control, whereby successful inhibition during response conflict is the result of a race between two independent processes: activation and inhibition (Gray, 1976; Logan & Cowan, 1984). If the former process is completed first, the response is executed; if the latter process is completed first, the response is withheld. Impairment of the latter process is thought

to be the primary cause of alcohol-induced increases in response disinhibition. Changes in response disinhibition are typically measured using a Stop-Signal or Cued Go/No-Go paradigm. The Cued Go/No-Go paradigm is commonly adopted as it shows how events preceding the response can influence inhibition and execution of the response (Marczinski & Fillmore, 2003b). In a Cued Go/No-Go task, a preliminary cue is presented prior to the 'go' or 'no-go' target to which the participant must respond or withhold responding, respectively. The cue indicates the probability of a 'go' or 'no-go' target; these cues have a high probability of correctly indicating the target (valid 'go' or 'no-go' cue) and a low probability of incorrectly indicating the target (invalid 'go' or 'no-go' cue). Deficient behavioural inhibition is inferred from the proportion of 'no-go' targets which generate a response (Ridderinkhof, van den Wildenberg, Segalowitz, & Carter, 2004). However, researchers often restrict the index of response disinhibition to the number of responses to 'no-go' targets preceded by an invalid 'go' cue. This measure focuses primarily on prepotent response inhibition, where participants must withhold a response which has already been initiated. The number of commission errors to 'no-go' targets on the Cued Go/No-Go task has been validated as a measure of impulsivity in high trait impulsivity groups (J. L. Smith, Johnstone, & Barry, 2004) and has been shown to predict binge alcohol use (Henges & Marczinski, 2012) and ad libitum laboratory-based alcohol consumption (Weafer & Fillmore, 2008).

2.7.3.2 Alcohol, Caffeine, and Response Disinhibition

Moderate to high alcohol doses (mean peak BrAC .050% to .102%) consistently impair pre-potent response inhibition on the Cued Go/No-Go task relative to placebo administration, evident via a significant increase in the proportion of commission

errors to invalid cued 'no-go' targets (Table 12). Alcohol administration typically does not impact commission error rates for valid cued 'no-go' targets. For example, Marczinski and Fillmore (2003a) showed that ingestion of moderate (mean peak BrAC .062%) and high (mean peak BrAC .094%) alcohol doses significantly increased invalid cued 'no-go' target commission error rate relative to placebo administration, whilst showing equivalent valid cued 'no-go' target commission error rates. These results suggest that alcohol has a differential effect on response disinhibition, primarily impairing performance when the response is pre-potent.

2.7.3.3 Alcohol, Energy Drinks, and Response Inhibition

These differential effects of alcohol administration on response disinhibition may not be appreciably altered by caffeine and ED co-ingestion. Combined administration of caffeine (2mg/kg to 4mg/kg) with alcohol (mean peak BrAC .102%) has typically caused equivalent impairment of response inhibition on Stop Signal (Attwood, Rogers, Ataya, Adams, & Munafo, 2012) and Cued Go/No-Go (Marczinski & Fillmore, 2003a) tasks compared to when alcohol is administered alone[17]. However, the results from one study indicate that the interactive effects of caffeine and alcohol may be dose-dependent; co-administration of a marginally higher caffeine dose (4.4mg/kg) relative to that administered in the aforementioned studies has been shown to reduce response inihibition impairment evident after a moderate alcohol dose (mean peak BrAC .073%) (Fillmore & Vogel-Sprott, 1999)[18]. Thus, it may be that interactive effects can be detected when higher doses of caffeine ($\geq$ 4.4mg/kg) are co-administered than those typically administered in this field of research.

[17] Note that the peak mean BrAC reflects that reported in the study by Marczinski and Fillmore (2003a); BrAC measurement was not undertaken in the study by Attwood et al. (2012).

Table 12

The Effect of Alcohol on Commission Rates to Valid and Invalid Cue 'No-Go' Targets in the Cued Go/No-Go Task for Non-Clinical Samples

Study	*N*[a]	Treatment Design[b]	Blinding[c]	Placebo/ Control Condition	Alcohol Dose[d]	Peak Mean BrAC (%)[e]	Valid Cued No-Go Target Commission Errors[f]	Invalid Cued No-Go Target Commission Errors[f]
Abroms, Fillmore, and Marczinski (2003)	40 (29)	Between-subject	ns (single blind)	Placebo	0.65g/kg	.083	=	↑^
Fillmore and Weafer (2004)	24 (12)	Within-subject	ns (single blind)	Placebo	0.65g/kg	.087	=	↑^
Fillmore, Marczinski, and Bowman (2005)	20 (12)	Within-subject	Double-blind	Placebo	0.65g/kg	.083	=	↑
Fillmore et al. (2008)	14 (7)	Within-subject	ns (single blind)	Placebo	0.65g/kg	.089	-	↑^
Fillmore and Weafer (2012)	40 (20)	Within-subject	ns (single blind)	Placebo	0.65g/kg	.058	-	↑
Marczinski and Fillmore (2003b)	12 (6)	Within-subject	Double-blind	Placebo	0.45g/kg	.062	=	↑
					0.65g/kg	.094	=	↑
Marczinski and Fillmore (2003a)	12 (6)	Within-subject	Double-blind	Placebo	0.65g/kg	.102	=	↑
Marczinski, Abroms, Van Selst, and Fillmore (2005)	24 (12)	Within-subject	Double-blind	Placebo	0.45g/kg	.055	=	↑^
					0.65g/kg	.083	↑^	↑^
Marczinski and Fillmore (2005b)	17 (9)	Within-subject	ns (single blind)	Placebo	0.45g/kg	.061	=	↑
					0.65g/kg	.084	=	↑
Marczinski and Fillmore (2005a)	24 (12)	Within-subject	Double-blind	Placebo	0.45g/kg	.053	=	↑^
					0.65g/kg	.084	↑^	↑^

Table 12 Continued

Study	*N*[a]	Treatment Design[b]	Blinding[c]	Placebo/ Control Condition	Alcohol Dose[d]	Peak Mean BrAC (g%)[e]	Valid Cued No-Go Target Commission Errors[f]	Invalid Cued No-Go Target Commission Errors[f]
Marczinski, Combs, and Fillmore (2007)	32 (16)	Within-subject	Double-blind	Placebo	0.65g/kg	.086	=	↑^
Ostling and Fillmore (2010)	32 (16)	Between-subject	Double-blind	Placebo	0.65g/kg	.081	-	↑
Weafer and Fillmore (2008)	26 (14)	Within-subject	ns (single blind)	Placebo	0.65g/kg	.085	-	↑
Weafer and Fillmore (2012a)	20 (10)	Within-subject	ns (single blind)	Placebo	0.65g/kg	.094	-	↑
Weafer and Fillmore (2012b)	48 (27)	Within-subject	ns (single blind)	Placebo	0.45g/kg 0.65g/kg	.059 .084	-	↑ ↑

Note. [a] The number in brackets represents the number of male participants. [b] The design is specified based on the alcohol dosing protocol (between or within subjects). [c] Single-blind indicates that participants were blind to treatment condition, double-blind indicates that participants and data collectors were blind to treatment condition, and 'ns' means that blinding was not specified, although participant blinding can be tentatively inferred from the use of a placebo condition. [d] The alcohol dose was calculated according to participant bodyweight (g/kg). [e] The breath alcohol concentration (BrAC) reported reflects the peak mean BrAC recorded for the study (overall or within a specific condition). [f] This column indicates whether alcohol administration significantly ($ps<.05$) increased (↑), decreased (↓), or did not alter (=) the number of commission errors related to placebo; in some instances the commission error rate for valid cued no-go targets was not assessed (-); these studies (with the exception of Marczinski & Fillmore, 2005a) all involved a visual Cued Go/No-Go task where the cue accurately signalled the target on 80% trials. ^ For the following studies a significant effect of alcohol relative to placebo/control was only recorded in specific conditions: Abroms et al. (2003): significant alcohol-induced increase present in the response suppression condition (complete inhibition of the response) and not in the response alteration condition (alternative overt response); Fillmore and Weafer (2004): significant alcohol-induced increase present for male and not for female participants; Fillmore et al. (2008): significant alcohol-induced increase in the response conflict condition (monetary reinforcement for quick responses to go targets and low rates of commission errors) and not in the no response conflict condition (no performance monetary reinforcement); Marczinski et al. (2005): significant alcohol-induced increase in the response engagement condition (inhibit response to depress response key) and not in the response disengagement condition (inhibit response to release response key); Marczinski and Fillmore (2005a): significant alcohol-induced increase for valid cued 'no-go' targets in low cue dependency condition (invalid cues preceded the targets on 40% trials) and not in the high cue dependency condition (invalid cues preceded the targets on 20% trials) and for invalid cued 'no-go' targets in the high cue dependency condition and not the low cue dependency condition; Marczinski et al. (2007): significant alcohol-induced increase evident only for binge drinkers and not for non-binge drinkers.

Similar outcomes were evident in the one study conducted examining the effect of the whole ED beverage in conjunction with alcohol on response disinhibition. Marczinski et al. (2011) reported equivalent commission error rates to valid and invalid cued 'no-go' targets when alcohol (0.65g/kg, mean peak BrAC .089) was consumed alone or co-ingested with a low ED dose (3.57mL/kg). This study adopted a between-subject design, whereby participants were allocated to one of four treatment groups (placebo, alcohol, ED, or AmED treatment; *n*=14 per group). Analyses showed no significant group difference in regards to demographics, self-reported history of alcohol and caffeine use, or baseline performance outcomes, suggesting that outcomes should not be attributable to systematic differences in group characteristics. However, replication of this study using a within-subject design could increase statistical power, decreasing individual variability in outcomes across treatment conditions.

2.7.4 Impulsive Decision-Making

2.7.4.1 Measurement of Impulsive Decision-Making

Impulsive decision-making is generally measured using a delay-discounting paradigm, where the participant makes multiple choices between smaller rewards delivered immediately versus larger rewards delivered at a later, delayed time point (Logue, 1988; Rachlin, 1990; Rachlin, Raineri, & Cross, 1991). From these procedures the pattern of reward devaluation as a function of the delay can be calculated. The primary outcome of interest is the indifference point; that is, the point at which the immediate and delayed amounts are of equal subjective value (i.e., the smallest immediate amount the participant chooses to receive instead of the larger delayed amount). The indifference point for each delay can be plotted to form

a discount function, with greater discounting of value by delay indicating greater impulsive decision-making. Delay-discounting has been verified as an index of impulsivity, with increased rates of delay-discounting evident in high trait impulsivity samples, including those diagnosed with substance dependence (Heil, Johnson, Higgins, & Bickel, 2006; Kirby, Petry, & Bickel, 1999; Petry) and pathological gambling (Petry, 2001b).

2.7.4.2 Alcohol and Impulsive Decision-Making

Human research involving delay-discounting typically comprises hypothetical question-based discrete choices between an immediate and delayed monetary reward (e.g., 'Would you prefer $3 now or $30 in six months?"). These studies have generally revealed mixed findings regarding the effect of alcohol on hypothetical delay-discounting (Table 13). Two studies have shown no effect of a low-to-moderate alcohol dose (mean peak BrAC approximately .037% to .076%) on hypothetical delay-discounting relative to placebo administration (Reynolds et al., 2006b; Richards, Zhang, Mitchell, & de Wit, 1999b). While Ortner, MacDonald, and Olmstead (2003) reported that a moderate alcohol dose (mean peak BrAC .074%) decreased delay-discounting relative to placebo and control conditions, the difference only trended towards significance and showed a small magnitude of effect[19]. In contrast, S. C. Reed et al. (2012) found that administration of a higher alcohol dose (mean peak BrAC .092%) significantly increased hypothetical delay-

[19] Calculation of the effect size for this comparison was based on the mean discounting (*k*) values provided in the article. These analyses indicated that there was a small magnitude increase in delay-discounting in the alcohol relative to placebo condition for the standard condition (Hedge's g =0.35) and the impelling cue (i.e., cue provoking impulsive choice) condition (Hedge's g =0.43), indicating that the alcohol-induced increase in delay-discounting may have little practical effect on behaviour.

discounting relative to placebo administration in a sample of heavy drinking women. The detection of alcohol-induced impairment at this higher dose suggests that the effects of alcohol on impulsive decision-making may be dose-dependent. This conclusion aligns with a strong body of animal research showing alcohol-induced increases in delay-discounting using operant procedures, where the reinforcement is received during the task (e.g., Evenden & Ryan, 1999; Poulos et al., 1998; Tomie et al., 1998). Previous research has revealed that questionnaire-based assessment produces slower rates of discounting relative to operant procedures (see Navarick 2004 for a review). Thus, the general absence of alcohol-induced impairment in the aforementioned studies could be attributed to the reduced sensitivity of hypothetical question-based discounting tasks.

Despite this evidence, only one published study (Reynolds et al., 2006b) has been conducted to date assessing the effects of alcohol on real-time discounting of tangible rewards. This study involved administration of the Experiential Discounting Task (EDT; Reynolds & Schiffbauer, 2004), a task where participants experience delay and reward decision consequences, and probability is incorporated into the delayed choice to better simulate real-life decision-making. Reynolds and Schiffbauer (2004) argue that this task has increased sensitivity to state-dependent changes in impulsive decision-making, as it has been theorised that delay to reward is perceived as aversive, and thus real-time experience of delay results in a preference for immediate rewards (Sonuga-Barke, Taylor, Sembi, & Smith, 1992). The aforementioned study showed dose-dependent effects of alcohol on impulsive decision-making, with greater delay discounting after a moderate (mean peak BrAC ~.076%), but not a low (mean peak BrAC ~.037%), alcohol dose (Reynolds et al., 2006b). Most notably, there was no significant effect of either alcohol dose on a

hypothetical question-based delay-discounting task administered in the same study. Consequently, the authors theorise that the high alcohol dose enhanced delay aversion, heightening preference for the immediate tangible reward, and increasing the rate of delay-discounting.

2.7.4.3 Alcohol, Energy Drinks, and Impulsive Decision-Making

Overall, these preliminary findings indicate dose-dependent effects of alcohol on delay-discounting when choice consequences are experienced in real-time. In contrast, there is a strong body of research showing that stimulant drugs (e.g., amphetamine, methylphenidate) decrease delay-discounting (de Wit, Enggasser, & Richards, 2002; Pietras, Cherek, Lane, Tcheremissine, & Steinberg, 2003; Shiels et al., 2009). Only one study to date has examined the effects of caffeine on delay-discounting, showing dose-dependent decreases in delay-discounting in rats following high dose administration (30 mg/kg) relative to saline administration (Diller, 2008). While the effects of caffeine on delay-discounting by humans remains relatively unexplored, the researchers theorised that caffeine administration increased self-controlled choice by heightening sensitivity to the reward amount, amplifying awareness of the discrepancy between outcomes. Based on this interpretation, it could be theorised that EDs may decrease delay-discounting, particularly in light of human research showing that administration of other ED ingredients (e.g., glucose) reduces delay-discounting (Wang & Dvorak, 2010). Whether any ED-related decreases in impulsive decision-making are sufficient to compensate for, or negate, alcohol-induced increases in this behaviour remains to be seen; to date, there has been no research assessing the effects of ED, alone or in combination with alcohol, on delay-discounting.

Table 13

The Effect of Alcohol on Discounting Rates (k value) for Immediate Versus Delayed Rewards in Hypothetical and Experiential Discounting Tasks for Non-Clinical Samples

Study	*N*[a]	Design[b]	Blinding[c]	Placebo/ Control	Task	Standard Amount[d]	Delay[e]	Probability[f]	Reim-bursement[g]	Alcohol Dose[h]	BrAC (%)[i]	Discounting[j]
Ortner et al. (2003)	76 (76)	Between -subject	ns	Control Placebo	Hypothetical	$10.00	0, 7, 30, 90, 180, 365 days	1.00	Received the money from one choice at actual delay	0.7g/kg	.074	↓*
S. C. Reed et al. (2012)	46 (0)	Within-subject	Double-blind	Placebo	Hypothetical	$11.00-$85.00#	7-180 days	1.00	One in six chance of receiving the reward on one trial	0.5g/kg	.056	↑^
										0.75g/kg	.092	↑^
Reynolds et al. (2006b)	24 (11)	Within-subject	Double-blind	Placebo	Hypothetical	$10.00	0, 2, 30, 180, 365 days	1.00	Received the money from one choice at actual delay	0.4g/kg	.037*	=
										0.8g/kg	.076*	=
					Experiential	$0.30	0, 15, 39, and 60 seconds	0.35	Received the total money accrued during task	0.4g/kg	.037*	=
										0.8g/kg	.076*	↑

Table 13 Continued

Study	*N*[a]	Design[b]	Blinding[c]	Placebo/ Control	Task	Standard Amount[d]	Delay[e]	Probability[f]	Reim-bursement[g]	Alcohol Dose[h]	BrAC (g%)[i]	Discounting[j]
Richards et al. (1999b)	24 (16)	Mixed	ns (single blind)	Placebo	Hypothetical	$10.00	0, 2, 30, 180, 365 days	1.00	Received the money from one choice at actual delay	0.5g/kg	.044	=
										0.8g/kg	.067	=
							No delay	0.25-1.00	Received the money from one choice at actual delay	0.5g/kg	.044	=
										0.8g/kg	.067	=

Note. [a] The number in brackets represents the number of male participants. [b] The design is specified based on the alcohol dosing protocol (between or within subjects); for the mixed design, participants were assigned to one of two active alcohol groups (0.5g/kg or 0.8g/kg), and then completed active and placebo conditions. [c] Single-blind indicates that participants were blind to treatment condition, double-blind indicates that participants and data collectors were blind to treatment condition, and 'ns' means that blinding was not specified, although participant blinding can be tentatively inferred in some cases from the use of a placebo condition. [d] The standard amount represents the small reward amount; participants have to decide between receiving this small adjusting amount versus a delayed/probabilistic reward; note that # indicates that the standard amount was not specified, and the amounts listed represented the potential minimum and maximum for standard and delayed rewards. [e] This column represents the hypothetical or real-time delay. [f] This column represents the probability that participants will receive the larger delayed amount. [g] This column represents the monetary amount participants received in reimbursement for task performance. [h] The alcohol dose was calculated according to participant bodyweight (g/kg). [i] The breath alcohol concentration (BrAC) reported reflects the peak mean BrAC recorded for the study (overall or at a set time point). [j] This column indicates whether alcohol administration significantly ($p<.050$) increased (↑), decreased (↓), or did not alter (=) the rate of discounting relative to placebo/control administration, with higher rates of discounting indicating greater impulsive decision-making; * indicates a trend towards significance ($p<.100$). Note that a hyperbolic fit was used for all studies with the exception of Richards et al. (1999b), who also used an exponential fit. Hyperbolic equation: $V = A / (1 + kD)$, where V is the current, subjective value of the delayed reward, A is the amount of the delayed reward, D is the delay to the reward and k is a free parameter representing the rate of devaluation of the delayed reward. ^ For Richards et al. (1999b): the authors reported a main effect of Alcohol Dose on delay-discounting, however these results should be treated with caution as breakdown analyses were not conducted to see whether both doses caused a significant increase in delay-discounting relative to placebo.

2.7.5 Impulsive Behavioural Consequences of Using Alcohol Mixed with Energy Drinks: Summary

Pharmacological-based state-dependent changes in behavioural impulsivity are theorised as a potential consequence of AmED consumption. This proposal is based on the finding that acute alcohol administration typically causes transient increases in certain aspects of impulsive behaviour. Thus, interactive effects of ED with alcohol in regards to impulsive behaviour may alter consumers' likelihood of engaging in risk-taking behaviour. However, the effects of co-ingesting ED may depend on the measure administered; impulsivity is a multi-faceted construct and previous research has shown that alcohol has differential effects on impulsivity depending upon the process being assessed. Impulsive response initiation, typically assessed using the IMT/DMT, has been shown to increase dose-dependently with alcohol, with alcohol-induced impairment detected following administration of moderate to high doses (BrAC ≥ .063%). Similarly, response disinhibition is generally exacerbated by moderate or higher alcohol doses (BrAC ≥ .050%), as evident by impaired inhibition of pre-potent responses on the Cued Go/No-Go task. Finally, preliminary evidence suggests that laboratory-based objective measures detect increased impulsive decision-making following administration of high alcohol doses (BrAC ≥ .076%), particularly when decision-making consequences are tangible and experienced during intoxication.

However, at present there is no strong empirical evidence base as to the potential impact of ED co-administration on alcohol-induced changes in behavioural impulsivity. Only one study has been conducted examining the effect of AmED relative to alcohol on response disinihibition in isolation; there has been no

comprehensive assessment of the differential effects of AmED on these aspects of impulsive behaviour, despite the recognition that this construct reflects several measurably different processes.

In order to address this oversight, the following research question must be addressed:

- Are any changes in objectively assessed impulsive behaviour (specifically impulsive response initiation, response disinhibition, and impulsive decision-making) evident when comparing the effects of an acute dose of AmED and alcohol in a controlled environment for the same individual?

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Chapter 3: Patterns of Use and Motivations for Consuming Alcohol Mixed with Energy Drinks

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3.1 Preface

This chapter outlines the first segment of results from an online survey regarding AmED use in the preceding six months, completed by a community-based convenience sample of Australian AmED consumers (*Study 1*). This manuscript specifically focuses on the consumption patterns and motivations reported by this sample. The study was undertaken to determine whether AmED consumption was associated with a high-risk drinking profile, as indicated by the quantity and frequency of use, beverage preferences, consumption context, and primary motivations driving beverage choice (*Question 1* and *2*). The manuscript filled a gap in the current literature, as the majority of studies focused on AmED consumption by university students (reducing generalizability to consumers in the general community) and assessed a restricted range of motivations relating primarily to intoxication-enhancement. It was intended that the results of this project would contribute to the evidence base for harm minimisation endeavours; that is, identification of primary consumption practices and motives for use would indicate the degree to which AmED regulation (i.e., availability, marketing, and cost) and consumer education may influence consumption practices. A copy of the survey is available in Appendix C.

3.2 Abstract

Objective: Use of alcohol mixed with energy drinks (AmED) is an increasingly prevalent trend. However, recent research has suggested that AmED use may result in increased alcohol consumption and engagement in risk-behaviour post-ingestion. While the majority of research has been focused on AmED use outcomes, there is a current paucity of data on the patterns of AmED use and motives for consumption.

Method: Four-hundred and three participants from an Australian community sample (*n*=244 females) aged 18 to 35 years who had consumed alcohol mixed simultaneously with energy drinks (EDs) in the preceding six months completed an online survey regarding use of EDs, alcohol, and AmED.

Results: While AmED sessions occurred relatively infrequently compared to alcohol sessions, the alcohol and ED quantity consumed in AmED sessions was significantly greater than recommended intake. Reports of AmED use context indicated that participants typically consumed AmED whilst engaging in heavy drinking in public venues. However, the primary motives for AmED use related to the situational context of use, functional and hedonistic outcomes, as well as the pleasurable taste; few participants reported using AmED to increase alcohol intake, mask intoxication, hide the flavour of alcohol, or simulate an illicit drug 'high'.

Conclusions: AmED users may be co-ingesting in a context and at a quantity which enhances the possibility of harmful alcohol outcomes, despite predominantly consuming AmED for the taste and functional and hedonistic outcomes. Strong endorsement of motives relating to ease of access and low cost price suggests that alcohol policy reform in relation to licensing restrictions may be necessary to minimise the risk of harm.

3.3 Introduction

While market size demographics and estimates of use indicate increased energy drink (ED) prevalence (Levy & Tapsell, 2007; Malinauskas et al., 2007), a new trend may be contributing to ED popularity: alcohol mixed with EDs (AmED). AmED use prevalence remains relatively unknown, as assessments have generally been restricted to regional non-probability sampling of university students. In two surveys of United States university students, 44% of participants reported lifetime AmED use (Marczinski, 2011) and 24% of recent alcohol consumers had used AmED in the preceding 30 days (O'Brien et al., 2008).

Emerging evidence suggests a potential for increased harms associated with this consumption practice. Co-ingestion may cause a discrepancy between actual and perceived intoxication, whereby AmED consumers underestimate alcohol-induced impairment (Ferreira et al., 2006). This reduced perception of intoxication has been argued to result in excess alcohol consumption and/or an increased likelihood of risk-taking behaviour (O'Brien et al., 2008; Oteri et al., 2007; Weldy, 2010). A study of Canadian university students showed that ED users consumed significantly more alcohol in AmED sessions than alcohol sessions (Price et al., 2010). However, AmED risk-taking findings are more equivocal. Field research by Thombs et al. (2010) revealed that bar patrons who had ingested AmED had a four-fold greater likelihood of reporting an intention to drive while intoxicated than non-AmED consumers. Conversely, a survey of Australian AmED users showed that the odds of engaging in a range of risk-behaviours was significantly less during AmED sessions relative to alcohol sessions (Peacock et al., 2012) .

However, there has been limited research into AmED consumption patterns and motives, as the majority of studies have been focused on ED use motivations, or on the consequences, rather than the causes, of AmED use. Marczinski (2011) reported that common AmED motivations included decreased fatigue, reduced time to intoxication, and greater alcohol intake. However, this study was restricted to an United States university student sample, limiting the generalisability of findings, as university student alcohol users generally display a unique drinking pattern relative to those in the general population (Ham & Hope, 2003).

Identification of common characteristics of consumption (i.e., quantity and frequency of AmED consumption, alcohol and ED beverage preferences, and AmED consumption context) may illuminate whether AmED is consumed in a manner and/or a setting which enhances the likelihood of increased alcohol consumption and risk-taking. Investigation of AmED consumption motives may identify whether consumers are ingesting AmED for the presumed stimulant effects of the ED, the interactive effect of alcohol and ED on intoxication sensation, or for alternative reasons. Consequently, the aim of the present study was to examine AmED consumption patterns and motivations in a sample of AmED users recruited from the general community.

3.4 Materials and Method

3.4.1 Participants

Between May and July 2011, 1,336 Australians aged 18 years or older participated in a self-administered internet-based survey of 10 to 30 minutes duration on the independent and combined use of alcohol and EDs. Participants were invited to

complete the survey regardless of their history of alcohol or ED use. The project received approval from the Human Research Ethics Committee (Tasmania) Network and was advertised via media reports, social network site postings, and notices exhibited in local venues. After submitting their responses participants could nominate to enter a prize draw to win an Apple iPad 2 via an independent secure webpage.

Following exclusion of data from participants who withdrew from the survey prior to survey completion (*n*=224); had 50% or more responses missing (*n*=3), reported an international residential status (*n*=9); and were outside the age range of the target ED consumer demographic (*n*=138) (Heckman et al., 2010); the final sample comprised 963 Australians aged 18 to 35 years.

Two-fifths (42%) of the final sample were identified as AmED users, as they reported: (i) consuming alcohol and EDs in the same drinking session in the preceding six months, and (ii) typically consuming the two constituents simultaneously (i.e., mixed within a single beverage) rather than successively (i.e., as separate beverages within the one drinking session). As the current analyses were restricted to AmED use, all references to the sample henceforth will refer to AmED users only (*N*=403).

3.4.2 Survey Content and Data Analysis

While the survey comprised 303 items assessing independent and combined alcohol and ED use, the current analyses are limited to data relating to: (i) AmED use frequency and quantity, (ii) AmED drink preferences, (iii) AmED use context, and

(iv) AmED use motivations, for the preceding six month period. Survey items were developed following an exhaustive literature review and extraction of recurrent themes in two 30-minute focus group sessions with six AmED users and four alcohol users aged between 21 and 47 (*M*=26.4, *SD*=7.6 years).

Participants indicated on a 5-point Likert scale how frequently 30 reasons motivated them to consume AmED and these responses were clustered into 'motivation absent' ('never' and 'less than half the time') and 'motivation present' ('half the time', 'more than half the time', 'all the time'). Exploratory factor analysis using the robust Weighted Least Squares (mean and variance adjusted) estimator with oblique (oblimin) rotation was conducted in Mplus to determine grouping of motivations; seven factors provided a good fit to the data (Comparative Fit Index = 0.981; Tucker-Lewis Index=0.967; root mean square error of approximation=0.044) and provided an interpretable factor structure. Items which clustered on the same factor (i.e., rotated factor loading >.33) indicated that the seven factors could be labelled: (i) functional motives (e.g., 'to feel more energetic'), (ii) intoxication/impairment motives (e.g., 'so I could drink more'), (iii) taste and sensation motives (e.g., 'because I like the taste of alcohol and energy drinks together'), (iv) illicit 'high' motives (e.g., 'as a legal alternative to illicit drugs'), (v) situational motives (e.g., 'because they was a discount drink special'), (vi) hedonistic motives (e.g., 'to have more fun'), and (vii) sociability motives (e.g., 'to feel more sociable'). Frequencies and means for categorical and continuous data were calculated using SPSS Statistics Version 19 (IBM, Somers, NY) and one-sample *t*-tests were applied where necessary.

3.5 Results

3.5.1 Demographics

The sample comprised predominantly young adult (*M*=23.1, *SD*=3.8, range 18-35 years) females (61%, 95%CI 55-65) who were generally well-educated, with the majority reporting Year 12 attainment (96%, 95%CI 93-97), and over nine-tenths completing (43%, 95%CI 38-48) or completed (52%, 95%CI 47-57) post-secondary school qualification(s). The sample also demonstrated a high employment rate, with two-fifths (39%, 95%CI 35-44) employed full-time and nearly one-half (45%, 95%CI 40-50) involved in part-time/casual employment. One-half reported typically using ED independently on a monthly basis (49%, 95%CI 44-54), with only one-fifth (19%, 95%CI 15-23) using EDs more than once per week. Additionally, the majority of the sample (85%, 95%CI 81-88) typically used one to two standard EDs (80 mg caffeine per standard drink) per consumption day; only 16% (95%CI 12-18) generally ingested three or more standard EDs. Independent alcohol use generally occurred on a fortnightly to thrice weekly basis (78%, 95%CI 74-82), with only one-tenth (12%, 95%CI 9-15) consuming alcohol more frequently. Typical intake during an alcohol only session was diverse, with one-third (33%, 95% CI 29-38) consuming four or fewer standard alcoholic beverages (10g alcohol per standard drink), nearly one-half (47%, 95%CI 42-52) consuming five to nine standard alcoholic drinks, and one-fifth (20%, 95%CI 16-24) consuming 10 or more standard alcoholic drinks.

3.5.2 Consumption Patterns

3.5.2.1 Frequency and Quantity

The majority (77%, 95%CI 73-81) of the sample consumed mixed beverages infrequently (i.e., monthly or less), with one-fifth (21%, 95%CI 17-25) reporting fortnightly to weekly use, and only a small proportion (3%, 95%CI 0-4) engaging in regular use (i.e., two or more days weekly). AmED sessions were also relatively infrequent compared to alcohol sessions, with three-quarters (73%, 95%CI 69-78) reporting that less than half of all alcohol drinking sessions involved AmED use; only one-quarter (27%, 95%CI 22-31) stated that at least half of all alcohol drinking sessions involved AmED. Furthermore, participants reported a lower proportion of AmED drinks to other alcohol drinks in AmED sessions, with 70% (95%CI 68-77) claiming that less than half their alcoholic drinks were AmED; only one quarter (27%, 95%CI 23-32) reported that at least half their alcoholic drinks were AmED.

Participants reported consuming 2.4 (*SD*=1.7, range 1-10) standard EDs in a typical AmED session and 3.0 (*SD*=2.3, range 1-15) standard EDs in their maximum AmED session. One-sample *t*-tests revealed that the Australian recommended maximum daily intake of two 250ml ED beverages (each containing 80mg caffeine; Food Standards Australia and New Zealand, 2009) was significantly exceeded in typical, $t(389)=4.15$, $p<.001$, 95% CI [0.2, 0.5], and maximum, $t(400)=9.23$, $p<.001$, 95% CI [0.8, 1.3] AmED sessions, with 33% and 46% of the sample exceeding this consumption threshold for each session type, respectively.

A similar pattern of excess consumption was evident in alcohol quantity estimates, with participants consuming 7.0 (*SD*=5.6, range 1-35) standard drinks in a typical

AmED session and 8.7 (*SD*=6.8, range 1-45) standard drinks in their maximum AmED session. The Australian National Health and Medical Research Council (2009) advises maximum consumption of four standard alcoholic drinks to minimise the risk of alcohol-related injury within a drinking session. However, one-sample *t*-tests revealed that this threshold was significantly exceeded in typical AmED sessions, $t(394)=10.94$, $p<.001$, 95% CI [2.5, 3.6], and maximum AmED sessions, $t(399)=13.99$, $p<.001$, 95% CI [4.1, 5.4], with 63% and 72% of the sample consuming five or more standard alcoholic drinks for each session type, respectively.

3.5.2.2 Drink Preferences

Nine-tenths (89%, 95%CI 85-92) of the sample reported using alcohol spirits as mixers in AmED beverages, and nearly half (48%, 95%CI 43-53) reported consuming liqueur; use of champagne, wine, and beer was minimal (<6%). These findings were corroborated by reports of preferred alcohol mixers, with over two-thirds (71%, 95%CI 66-75) preferring spirits (e.g., vodka) and one-quarter (27%, 95%CI 23-32) preferring liqueur (e.g., Jägermeister). The preponderance (93%, 95%CI 90-96) of those who preferred spirits identified vodka as the primary spirit mixer, with few participants typically using gin (2%, 95%CI 0-4) or whisky (2%, 95%CI 0-4). Similarly, the majority of the sample typically used one ED mixer, Red Bull® (standard: 83%, 95%CI 79-87; sugar-free: 6%, 95%CI 4-8); only a small proportion reported typical use of Mother® (5%, 95%CI 3-7), V® (3%, 95%CI 2-5), or other products (3%, 95%CI 1-5).

3.5.2.3 Use Context

Over three-quarters of the sample typically consumed their first AmED beverage during the evening, with 27% (95%CI 23-31) and 52% (95%CI 47-57) commencing AmED consumption between 6:01pm and 9:00pm and 9:01pm and12:00am, respectively. However, 15% (95%CI 11-18) reported commencing AmED ingestion post-midnight (12:01am-3:00am). This late-night initiation of AmED use may be attributed to the typical consumption location, with over two-thirds typically consuming AmED in nightclubs (42%, 95%CI 37-47) or bars and pubs (30%, 95%CI 26-35); only one-fifth reported private residences (private party 11%, 95%CI 8-14; consumer's home: 10%, 95%CI 7-13) as their typical consumption location. AmED use was generally associated with excess alcohol ingestion, with two-thirds (66%, 95%CI 61-71) reporting normally consuming AmED in maximum, rather than typical, alcohol consumption sessions.

3.5.3 Motivations for Use

Motivations for AmED use are displayed in Table 1. Improved functionality was a primary motive for co-ingestion, with three-quarters of the sample reporting use for energetic purposes, and over half consuming AmED to extend attendance at public venues and drinking establishments. Not surprisingly, taste and sensation motives played a part in beverage choice, with over two-thirds of the sample endorsing the combined taste of alcohol and EDs as an enticement for consumption. Situational motives were also a predominant factor; preference for specialty mixed drinks (e.g., Red Bull® and vodka, Jägerbombs) was reported by three-fifths of the sample, and over two-fifths reported that sharing AmED with drinking companions, AmED availability, and AmED price discounting influenced their beverage choice.

However, only one-fifth reported using AmED to mask the flavour of alcohol. In regards to the hedonistic motives, nearly one-half of the sample reported consuming AmED to have more fun, while one-third of the sample reported using AmED to 'get more drunk'.

Lower rates of endorsement were evident for intoxication and impairment, illicit 'high', and sociability motives. The majority of AmED users did not endorse items regarding reduced internal experience and/or physical manifestation of intoxication. However, one-fifth of the sample used AmED to increase alcohol intake. Only one-tenth of the sample reported drinking AmED to achieve an intoxication experience similar to illicit drug use, while one-third indicated that facilitated sociability was a factor in beverage choice. Pearson's χ^2 test revealed no significant differences in AmED use motivations according to sex (*p*s>.05).

3.6 Discussion

The aim of the present study was to determine AmED consumption patterns and motivations in a group of users recruited from the general community. While AmED sessions reportedly occurred less frequently than alcohol sessions, alcohol and ED quantities consumed in AmED sessions significantly exceeded recommended intake guidelines. However, it cannot be presumed that this excess alcohol quantity reflects only the alcohol consumed in AmED beverages, as participants generally reported that, when drinking AmED, not all of the beverages consumed in that session contained ED.

Table 1

Endorsement of Motivations for AmED Consumption (95%CI in parentheses)

Motivations According to Theme Area	**% of Participants Endorsing Motivation as Present (95% CI)[a]**
Functional Motives:	
To feel more energetic	70 (65-74)
So I could stay out later	54 (49-59)
To be more alert	45 (41-50)
To improve my mood	31 (26-35)
Intoxication/Impairment Motives:	
So I could drink more	20 (16-24)
To be able to concentrate more	17 (13-21)
To decrease boredom	13 (10-17)
To feel less drunk	12 (9-15)
To look less drunk	8 (5-10)
To avoid getting a hangover	6 (4-8)
Taste and Sensation Motives:	
Because I like the taste of alcohol and energy drinks together	69 (65-74)
Because I like the taste of energy drinks	57 (52-62)
Because I like the combined effect	49 (44-54)
'High' Motives:	
As a legal alternative to illegal drugs	10 (7-13)
To simulate or mimic the effects of illegal drugs (e.g., ecstasy)	6 (4-8)
Situational Motives:	
Because they are ingredients in a drink (i.e. Jägerbomb)	72 (70-77)
Because the person/group of people I was with were drinking them (e.g., had shots together, shared a jug of alcohol and energy drink mixed together)	53 (48-59)
Because energy drinks were available to drink with alcohol	51 (46-56)
Because there was a discount drink special	45 (40-50)
Because it was available at a party	44 (39-49)
Because other people I knew were drinking them	40 (35-45)
Because energy drinks are a popular drink to mix with alcohol	39 (34-44)
To hide the flavour of alcohol	22 (20-28)

Table 1 Continued

Motivations According to Theme Area	% of Participants Endorsing Motivation as Present (95% CI)[a]
Hedonistic Motives:	
Because someone bought it for me	53 (49-58)
To have more fun	46 (41-51)
To get a bigger buzz	42 (37-46)
To get more drunk	32 (28-37)
For the thrill	20 (16-24)
Sociability Motives:	
To feel more sociable	30 (25-34)
To feel more confident	16 (12-19)

Note. [a] The percentage represents the number of AmED consumers who reported each motivation for at least half of all AmED (alcohol mixed with energy drink) sessions in the preceding six months. Figures in brackets represent the 95% confidence interval.

Notwithstanding, the risks associated with excess alcohol consumption may be enhanced by the reported typical locale and time of day for AmED use, as late-night drinking and alcohol consumption in public drinking establishments has been associated with an increased risk of heavier alcohol consumption and alcohol-related aggression (Rossow, 1996; Single & Wortley, 1993; Stockwell et al., 1993). Coupled with the finding that the majority of AmED users co-ingest during 'heavier' alcohol consumption sessions, these indices of consumption suggest a potentially hazardous drinking environment for AmED use. However, caution should be employed when interpreting these results in light of alcohol only consumption, as a comparison of the relative riskiness of consumption patterns for AmED and alcohol sessions was not undertaken.

Predominant AmED consumption motives related to the functional outcomes, with the majority citing increased energy and ability to stay out later as a factor in AmED beverage choice. While only a small proportion consumed AmED to increase their

sociability and boost self-confidence, approximately two-fifths of the sample reported being driven by hedonistic motives in their beverage choice. However, this pleasure-seeking was generally within the boundaries of behavioural control, with only one-tenth endorsing motives regarding seeking a 'high' similar to illicit drug use. Use of AmED to enhance or reduce intoxication and subsequent impairment was minimal; while one-fifth used AmED to be able to drink more, only one-tenth chose AmED as a means of reducing the experience or manifestation of intoxication. Overall, the majority of surveyed AmED users appear driven primarily by the functional and hedonistic consumption outcomes; only a small subset reported positioning themselves in a situation of increased risk by attempting to increase alcohol intake, heighten alcohol-induced impairment, and/or experience a 'high' similar to illicit drug use.

Further support for this premise is evident in regards to taste motives, with the majority citing the pleasurable taste of AmED as a factor in beverage choice; only one-fifth reported co-ingesting to disguise alcohol's taste. Increased Australian excise taxes on ready-to-drink spirit-based products ("alcopops") were partly driven by the belief that the "sugary sweet" beverages permitted increased alcohol consumption by disguising the flavour of alcohol (Chikritzhs et al., 2009; Mart, 2011). The current results suggest that the same principle may not apply to AmED use, or at least, that consumers do not explicitly report this motivation. Overt offers of alcohol and modelling of peers' beverage choices, motives endorsed by over two-fifths of the present sample, have been associated with excess alcohol consumption, particularly in university student samples (Borsari & Carey, 2001). Additionally, approximately one-half of those surveyed reported AmED physical availability and

drink discounting as motivations for use. These findings are concerning in regards to potential increased alcohol consumption and risk-taking following AmED consumption, as a strong body of literature supports the inverse relationship between price of alcohol and level of consumption (e.g., Wagenaar, Salois, & Komro, 2009). Furthermore, drink discounting has been consistently linked to greater intoxication amongst bar patrons (Thombs et al., 2008; Thombs et al., 2009). AmED price and availability regulation is difficult to achieve in off-licence premises as the two constituents may be purchased as separate beverages. However, legislation regarding the hours of sale, retail price, drink discounting, and marketing and promotion of AmED could be enforced in licensed drinking venues which trade in these beverages (Loxley et al., 2005). While these measures have generally been effective in reducing alcohol consumption and related harm, their potential impact on reducing any harms that may arise from alcohol or AmED consumption remains unexplored. Western Australia Liquor Licensing has banned the sale of AmED beverages in Perth's licensed venues from midnight. However, there is currently no data on this strategy's effectiveness on reducing health harms or public order problems due to the limited implementation period (i.e., 2011).

While caution should be employed when interpreting the present study's results as data was self-reported, certain procedures were implemented to ensure anonymity and minimise response bias. The survey was web-based to allow participants to complete the survey independently, self-identifying data was not collected, and contact details for prize draw entry were entered on a secure, independent webpage. Additionally, while it cannot be assumed that the current sample is representative of the Australian general population (participants were self-selected via research

advertisements), the current results do provide insight into AmED consumption patterns and motives beyond the university student sample.

In conclusion, while AmED sessions are reportedly relatively infrequent compared to alcohol sessions, the alcohol and ED quantity consumed within the session, and the consumption context, may increase the potential for adverse outcomes. Despite this, the majority of consumers appear driven in beverage choice by the taste, situational context of use, and the functional and hedonistic AmED outcomes; only a small proportion of consumers ingest AmED to increase alcohol intake, reduce the experience of intoxication, or experience a 'high' similar to illicit drug use. However, strong endorsement of motivations regarding increased drink availability and discounted price suggests that alcohol policy reform may minimise the risk of harm post-AmED ingestion.

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Scientific Conference, 2011, and the 35th Annual Research Society on Alcoholism Scientific Meeting, 2012.

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Chapter 4: Self-Reported Retrospective Physiological, Psychological, and Behavioral Risk-Taking Consequences of Alcohol and Energy Drink Co-Ingestion

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4.1 Preface

This chapter outlines the results from the second section of the online survey (*Study 1*) completed by the convenience sample of community-based Australian AmED consumers. These results relate specifically to the self-reported physiological, psychological, and behavioural outcomes of AmED and alcohol consumption in the preceding six months. The aim of this manuscript was to determine whether consumers retrospectively reported an appreciable increase in alcohol-related harms when co-ingesting alcohol with ED relative to when they had consumed alcohol without ED (*Question 3*). To date, this is the first published study comprising a within-subject comparison of AmED and alcohol consequences in a community-based sample. The outcomes in this manuscript, coupled with the results reported in *Chapter 3*, illustrate the typical drinking experience of Australian AmED consumers, showing that AmED use may have a two-fold effect, reducing sedation side-effects and increasing stimulation side-effects. Furthermore, it reinforces the need for research investigating the presumed effects of AmED, highlighted by the discrepancy between theorised and reported behavioural outcomes. A copy of the survey is available in Appendix C.

A Letter to the Editor was published by Rossheim et al. (2013) in *Alcoholism: Clinical and Experimental Research* in response to this manuscript. The response to this letter by Rossheim and colleauges, authored by the Candidate, is available in Appendix D (Peacock et al., 2013b).

4.2 Abstract

Background: The increasingly popular practice amongst adolescents and young adults of consuming alcohol mixed with energy drinks (AmED) has raised concern regarding potential increases in maladaptive drinking practices, negative psychological and physiological intoxication side-effects, and risky behavioural outcomes. Comparison of user types has revealed that AmED users report engaging in more risk-taking behaviour relative to alcohol users. However, the comparative likelihood of risk-taking according to session type (i.e., AmED versus alcohol session) remains relatively unknown. Thus, the current study was designed with the aim of establishing the subjective physiological, psychological, and behavioural risk-taking outcomes of AmED consumption relative to alcohol consumption for AmED users drawn from the community.

Method: Between May and June 2011, 403 Australians aged 18 to 35 who had consumed AmED and alcohol only in the preceding six months completed a 10-30 minute online survey about their use of these substances.

Results: Despite participants consuming a significantly greater quantity of alcohol in AmED sessions compared to alcohol sessions, the odds of participants experiencing disinhibition and engaging in 26 risk behaviours were significantly lower during AmED sessions relative to alcohol sessions. Similarly, the odds of experiencing several physiological (i.e., speech and walking difficulties, nausea) and psychological (i.e., confusion, exhaustion, sadness) sedation outcomes were less during AmED sessions compared to alcohol sessions. However, the odds of enduring physiological (i.e., heart palpitations, sleep difficulties, agitation, tremors, jolt and crash episodes, and increased speech speed) and psychological (i.e., irritability,

tension) outcomes potentially related to over-stimulation were significantly greater during AmED sessions than alcohol sessions.

Conclusions: Co-ingestion may provide a double-edged effect. The increased stimulation from energy drinks may reduce some intoxication-related sedation side-effects by increasing alertness. However, it could also lead to negative physiological side-effects associated with over-stimulation. Notwithstanding any stimulatory effects of energy drinks, risk and negative effects of excessive alcohol consumption were present in both session types. However, the odds of engaging in risk-taking were less during AmED sessions relative to alcohol sessions. Objective measurement of behavioural risk-taking via laboratory-based measures could confirm the causal link between AmED consumption and risk-taking.

4.3 Introduction

Market size demographics and estimates of use indicate increasingly widespread energy drink (ED) consumption, particularly amongst the adolescent and young adult demographic (Heckman et al., 2010; Levy & Tapsell, 2007; Reissig et al., 2009). However, over the last decade a new ED consumption pattern has become increasingly popular: alcohol mixed with ED (AmED). AmED use prevalence estimates have generally been based on regional non-probability sampling of university student populations, with 24% of an American university student sample reporting AmED consumption in the preceding month (O'Brien et al., 2008), and 48% of an Italian university student sample reporting lifetime AmED use (Oteri et al., 2007).

The use of AmED may be based on a perceived improvement in alcohol-induced physical and cognitive impairment (Ferreira et al., 2006; Weldy, 2010). The presumed interaction of alcohol and EDs is based on the premise of oppositional global pharmacological effects, whereby the stimulatory nature of the ED is thought to negate the depressant effects of alcohol (Ferreira et al., 2006). Objective measurement of the effects of AmED on performance generally contradict this hypothesis, with the majority of research yielding no significant reduction of alcohol-induced impairment in performance after co-ingestion relative to alcohol only (Ferreira et al., 2006; Marczinski et al., 2011; Marczinski et al., 2012); only Marczinski et al. (2011) have reported ED attenuation of alcohol-induced impairment during measurement of response execution in a Cued Go/No-Go task.

Indeed, research on the subjective psychological, physiological, and behavioural risk-taking outcomes of AmED use presents a divergent profile of alcohol and EDs' interactive effects. Measurement of perceived psychological outcomes has generally been restricted to mood state ratings of stimulation (e.g., 'elated', 'energised') and sedation (e.g., 'down', 'sedated'). However, the lack of statistically significant difference in mood states recorded following AmED and alcohol ingestion suggest no interactive effect of EDs on alcohol-induced psychological changes (Marczinski et al., 2011). In contrast, support for the oppositional global effects of the two constituents is evident from measurement of perceived physiological side-effects, with participants reporting reduced headache, weakness, and dry mouth sensation intensity after AmED relative to alcohol ingestion (Ferreira et al., 2006). These results suggest that co-ingestion of EDs with alcohol may result in reduced perception of some alcohol-induced physiological side-effects, despite generally similar outcomes on objective performance measures.

The discrepancy between objective and subjective measures of intoxication could reflect a reduced ability to accurately detect level of impairment after AmED, which may result in continued consumption of alcohol and an increased likelihood of engaging in risk-taking behaviours (O'Brien et al., 2008; Oteri et al., 2007). For example, Canadian university students who identified as ED users reported consuming significantly more alcohol in AmED drinking sessions compared to alcohol sessions (Price et al., 2010). Additionally, O'Brien et al. (2008) found that United States university students who reported using AmED had a significantly higher prevalence of engaging in six alcohol-related consequences, including being

taken or taking advantage of another sexually, riding in a vehicle with the driver under the influence of alcohol, or being hurt, injured, or requiring medical treatment.

However, individuals who choose to consume AmED may systematically differ from alcohol users in their level of risk-taking propensity. Thus, although O'Brien et al.'s (2008) findings imply greater risk-taking by AmED users, a causal link between co-ingestion and behavioural outcomes cannot be inferred as reporting was not session-specific (i.e., risk-taking in AmED sessions versus alcohol sessions). However, few researchers have examined subjective behavioural risk-taking according to session type. This is particularly concerning considering ED marketing and cross-promotional strategies, whereby product branding and extreme sport sponsorship bolsters the adrenaline-charged, thrill-seeking connotations of ED consumption, allowing users to vicariously partake in risky, extreme behaviour through their own consumption (Heckman et al., 2010; Miller, 2008b). These ED marketing strategies target a high risk, sensation-seeking demographic. L. Berger et al. (2011) reported that hazardous alcohol drinkers had almost four-fold increased odds of reporting AmED use relative to nonhazardous drinkers. Similarly, Brache and Stockwell (2011) found in a survey of Canadian university students that frequent AmED consumers had almost twice the odds of driving while intoxicated, being a passenger of an intoxicated driver , or being hurt or injured compared to less frequent AmED consumers, even after controlling for individual differences (i.e., risk-taking propensity and drinking behaviour). However, a causal relationship between AmED and risk-taking cannot be inferred from these results, as a comparison of risk-taking while under the influence of AmED relative to alcohol only was not undertaken. Field research by Thombs et al. (2010) has showed that bar patrons who have

consumed AmED had a four-fold increased likelihood of reporting an intention to drive a motor vehicle while intoxicated than those who had not consumed AmED. Furthermore, Woolsey et al. (2010) found that American university student athletes who used AmED were significantly more likely to expect to act aggressively, and drive a motor vehicle during AmED sessions compared to alcohol sessions. However, Woolsey et al. (2010) did not find a significant difference between session types in regards to AmED users' expectation of taking risks and engaging in physical violence.

Thus, the existing research generally suggests that risk-taking related to aggressive behaviour, risky driving practices, and physical injury may be greater in AmED consumers compared to alcohol consumers, and after co-ingestion relative to independent alcohol consumption. However, the comparative likelihood of risk-taking behaviour by AmED users during alcohol and AmED sessions across a broader array of specific risk-behaviours remains relatively unknown. Additionally, the current paucity of data regarding the psychological, physiological, and behavioural risk-taking outcomes of AmED ingestion for other than university student consumers suggests that this also requires investigation, as alcohol users within this demographic generally display a unique drinking pattern relative to those in the community (Ham & Hope, 2003). As the nature of the outcomes under investigation (e.g., risk-taking behaviours related to sexual practices, illicit drug use, illegal driving practices) may be sensitive for participants and thus subject to under-reporting, a self-administered anonymous web-based survey was proposed to increase the likelihood of accurate reporting (Kreuter, Presser, & Tourangeau, 2008). The aim of undertaking this survey was to determine the subjective psychological,

physiological, and behavioural risk-taking consequences of AmED and alcohol only ingestion in a sample of AmED users recruited from the Australian community.

4.4 Materials and Methods

4.4.1 Participants and Procedure

Between May and July 2011, 1,113 participants aged 18 years or older completed a self-administered online internet-based survey on independent and combined ED and alcohol consumption patterns. Participants were invited to complete the survey regardless of their history of alcohol or ED use and were recruited via posters displayed in the greater Hobart (Tasmania, Australia) area in cafes, bars, nightclubs, and university campuses, as well as media reports and posts on internet forums and social networking sites. Survey completion time was dependent on the participants' history of alcohol and ED use, varying between 10 and 30 minutes. After submitting their responses, participants could redirect to a secure webpage and enter a prize draw to win an Apple iPad 2. The project was granted ethics approval by the Human Research Ethics (Tasmania) Network.

Following exclusion of data from participants with 50% or more responses missing (n=3); those who reported an international residential status (n=9); and those outside the age range of the target ED market (18 to 35 years; Heckman et al., 2010) (n=138), the full sample comprised 963 Australian males and females aged 18 to 35 years. Two-fifths (42%) of the sample were identified as AmED users, as they reported: (i) consuming alcohol and EDs in the same drinking session in the preceding six months, and (ii) typically consuming the two constituents simultaneously (i.e., mixed within a single beverage) rather than successively (i.e., as

separate beverages within the one drinking session). As the current analyses were restricted to AmED users, all references to the sample will refer to this 42% of the sample, that is, AmED users only (*N*=403).

4.4.2 Survey Design and Content

Following an exhaustive review of the literature, potential items and response options were devised based on the literature, standardised questionnaires (physiological items: visual analogue scales (Ferreira et al., 2006)); psychological items: Profile of Mood States (POMS; McNair et al., 1979) and Biphasic Alcohol Effects Scale (BAES; Martin et al., 1993)), and extraction of recurrent themes apparent in two 30-minute focus group sessions with six AmED users and four alcohol users aged between 21 and 47 (*M*=26.4; *SD*=7.6 years). Item refinement was achieved via iterative application of the Question Appraisal System (Willis & Lessler, 1999). The online format of the survey was pilot-tested by three volunteers. The final survey consisted of 303 items assessing: (i) patterns of independent and combined ED and alcohol use, (ii) motivations for AmED use, (iii) physiological, psychological, and behavioural outcomes of acute alcohol and AmED intoxication, (iv) licit and illicit drug use, (v) demographics, and (vi) trait impulsivity. The current analyses were limited to the patterns of independent and combined use, as well as AmED use outcomes.

In relation to the current analyses, participants who identified as AmED users were asked to indicate: (i) the typical frequency of ED, alcohol, and AmED consumption, and (ii) the quantity of alcohol and/or EDs consumed in typical alcohol, ED, and AmED drinking sessions. Participants were then asked to indicate on a 5-point Likert

scale (ranging from ‘never’ to ‘all the time’) how frequently they had experienced 17 physiological side-effects (e.g., ‘I had heart palpitations’) and 21 mood states in the previous six months during: (i) AmED drinking sessions and (ii) alcohol drinking sessions. The mood states selected for inclusion represented several themes areas: stimulation (e.g., ‘I felt alert’), contentment/sociability (e.g., ‘I felt friendly’), sedation (e.g., ‘I felt exhausted’), anti-sociability (e.g., ‘I felt irritable’), and impulsivity (e.g., ‘I felt daring’).

Finally, AmED users were asked to report using a dichotomous response format (yes, no) whether they had engaged in 26 risk-behaviours in the preceding six months during: (i) AmED drinking sessions, and (ii) alcohol drinking sessions. Risk behaviours selected represented several theme areas: licit and illicit drug use (e.g., ‘I drank more alcohol than I planned to’), sexual practices (e.g., ‘I had sex with someone I had only recently met’), motor vehicle behaviour (e.g., ‘I did not wear a seatbelt while I/someone else was driving a vehicle), financial outcomes (e.g., ‘I gambled’), aggressive behaviour (e.g., ‘I grabbed, pushed, slapped, punched and/or shoved someone’), mental and physical distress, injury, or harm (e.g., ‘I acted in a way that resulted in me experiencing humiliation or embarrassment’), and other antisocial behaviour (e.g., ‘I was asked to leave or kicked out of a club/bar/pub’). AmED users who endorsed each risk behaviour during an AmED session indicated the degree to which they attributed engagement in the behaviour to ingestion of EDs with alcohol on a 4-point Likert scale ranging from ‘not at all’ to ‘all’, as an indication of their perception of the link between AmED use and risk-taking. A copy of the survey can be made available on request from the corresponding author.

4.4.3 Data Analysis

Frequencies and means for categorical and continuous demographic data were calculated using SPSS Statistics Version 19 (IBM, Somers, NY). Responses to physiological and psychological AmED and alcohol outcome items were clustered into 'side-effect absent' ('never' and 'less than half the time') and 'side-effect present' ('half the time', 'more than half the time', and 'all the time') to provide 2 x 2 contingency tables (AmED Side-Effect: Present/Absent; Alcohol Side-Effect: Present/Absent). Odds ratios were calculated using Comprehensive Meta-Analysis Version 2 (Biostat, Englewood, NJ) to determine the relative likelihood of each behavioural, physiological, and psychological outcome during AmED and alcohol sessions, with alcohol session functioning as the reference category. Participants who reported using only AmED in the preceding six months (i.e., no alcohol only sessions) (n=18) were excluded from odds ratio analyses. Responses to the AmED session attribution item were grouped into attribution absent ('not at all' and 'somewhat') and attribution present ('mostly' and 'all').

4.5 Results

4.5.1 Demographics

The majority of the sample were female (61%), with a mean age of 23.1 years (SD=3.8, range 18-35 years). Participants were relatively well-educated, with reported Year 12 attainment considerably higher than national indicator data (96% and 78%, respectively) (Australian Bureau of Statistics, 2011). The majority of participants had completed (52%) or were currently completing (43%) post-

secondary school qualification(s) and were engaged in full-time (39%) or part-time/causal employment involving 30 hours or less of paid work per week (45%).

4.5.2 Alcohol, Energy Drink, and Alcohol Mixed with Energy Drink Use: Frequency and Quantity

As evident in Figure 1, the frequency of combined ingestion was generally less than independent alcohol and ED ingestion. While AmED was typically ingested on a monthly or less basis, EDs were generally consumed on a weekly to monthly basis and alcohol was generally consumed on a fortnightly to thrice weekly basis.

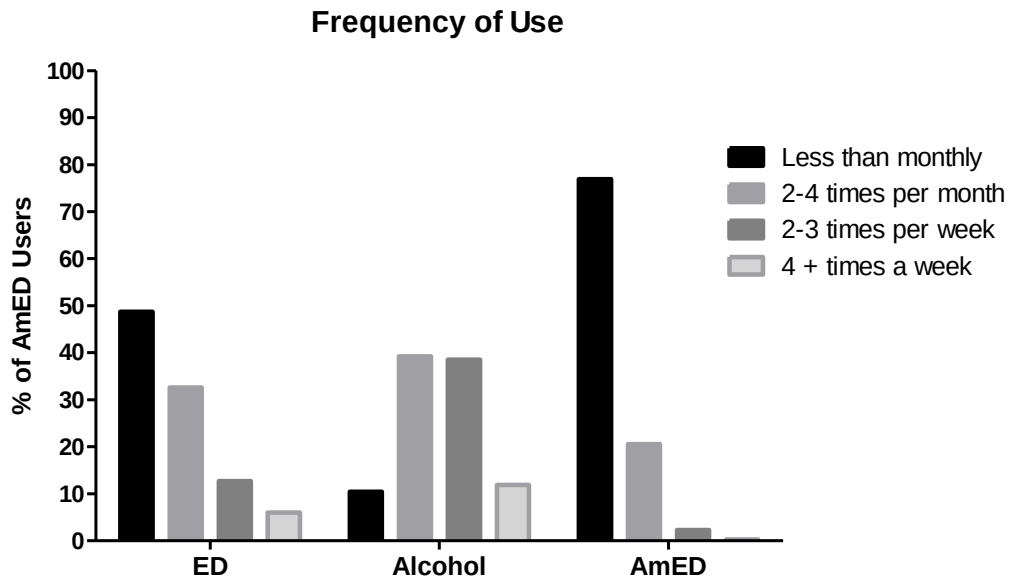

Figure 1. Typical frequency of ED (energy drink), alcohol, and AmED (alcohol mixed with energy drink) drinking sessions.

Independent ED use was generally quite judicious, with the majority of participants (85%) reporting typical consumption of one or two standard EDs per session; only 16% of participants reported consumption in excess of the Australian recommended daily intake guidelines (i.e., maximum consumption of two 250ml ED beverages each containing 80mg caffeine) (Food Standards Australia and New Zealand, 2009). Participants reported an average consumption of 2.4 (*SD*=1.7, range=1-10) standard EDs in AmED sessions. While comparison of ED quantities between session type was not possible, a one-sample *t*-test revealed that the quantity of ED ingested in AmED sessions significantly exceeded the aforementioned recommended daily intake, $t(389)=4.15$, $p<.001$, 95% CI [.19, .52], with 33% reporting typical consumption of three or more standard EDs during AmED sessions.

The typical number of standard alcoholic drinks was greater in the case of co-ingestion relative to independent ingestion, with a paired samples *t*-test revealing that a significantly greater quantity of alcohol was consumed in AmED sessions (*M*=7.1, *SD*=5.6) compared to alcohol sessions (*M*=6.5, *SD*=4.8), $t(386)=2.53$, $p=.012$, 95% CI [-1.16, -0.15]. However, these results should be interpreted judiciously as, given the lower frequency of AmED sessions, estimates of alcohol quantities are based on slightly different time reference periods (i.e., one month reference period for use in alcohol sessions and six month reference period for use in AmED sessions). One-sample *t*-tests revealed that the recommended threshold for alcohol-related injury risk-reduction in a drinking session (i.e., maximum of four standard drinks) (National Health and Medical Research Council, 2009) was exceeded in alcohol, $t(394)=10.20$, $p<.001$, 95% CI [1.99, 2.94], and AmED sessions, $t(394)=10.94$,

p<.001, 95% CI [2.51, 3.61], with 61% and 63% of participants consuming five or more drinks per typical alcohol and AmED session, respectively.

4.5.3 AmED and Alcohol Behavioural Risk-Taking Outcomes

Table 1 presents the relative likelihood of engagement in risk-behaviours during AmED and alcohol sessions based on the reported intoxicated risk-taking behaviour by participants in the preceding six months. Overall, risk-taking behaviour was higher across all categories in alcohol sessions relative to AmED sessions. This was supported by examination of the odds ratios, which indicated that participants had significantly lower odds of engaging in all 26 risk behaviours in AmED sessions relative to alcohol sessions. However, these results do not imply the complete absence of risk-taking in AmED sessions, with the reported rate of risk-taking by participants during AmED session typically within 25 percentage points of alcohol sessions (Table 1).

Table 1 also displays the percentage of participants who attributed their engagement in the risk behaviour during an AmED session to consuming EDs with alcohol. Where inferences regarding attributions were not hampered by small sample sizes, less than one-fifth attributed their risk-taking behaviour during AmED sessions as due to co-ingestion of EDs with alcohol.

Table 1

Percentage (%) and Odds Ratio for Engagement in Risk Behaviours in AmED Sessions Relative to Alcohol Sessions

Risk Behaviour	***N***	**% Alcohol Session[a]**	**% AmED Session[a]**	**Odds Ratio[b] (95% CI)**	**% Attribute to ED [c]**
Licit and Illicit Drug Use:					
Smoked cigarettes	380	45	32	0.59 (0.51, 0.69)***	12
Drank more alcohol than planned	374	75	62	0.54 (0.43, 0.68)***	16
Used legal drugs for recreational purposes	377	14	8	0.56 (0.44, 0.72)***	0.0
Used illegal drugs	376	29	15	0.42 (0.34, 0.53)***	2
Sexual Practices:					
Had sex with someone recently met	374	33	19	0.47 (0.38, 0.58)***	10
Did not use contraception	373	27	16	0.51 (0.41, 0.62)***	5
Was touched in an unwanted sexual way	378	15	7	0.41 (0.29, 0.57)***	#
Touched someone in an unwanted sexual way	380	6	3	0.56 (0.37, 0.85)***	8
Driving Behaviour:					
Drove while over legal alcohol limit	375	15	4	0.21 (0.13, 0.34)***	15
Passenger while driver over the legal alcohol limit	370	20	5	0.24 (0.16, 0.36)***	10
Seatbelt omission	378	9	4	0.38 (0.25, 0.58)***	0
In a vehicle with an illegal passenger number	380	25	10	0.34 (0.26, 0.46)***	5
In a vehicle exceeding speed limit by at least 10%	380	8	5	0.58 (0.42, 0.81)**	22
Financial Outcomes:					
Spent more money than planned	376	75	59	0.47 (0.37, 0.60)***	15
Gambled	377	24	10	0.34 (0.25, 0.46)***	6

Table 1 Continued

Risk Behaviour	*N*	% Alcohol Session[a]	% AmED Session[a]	Odds Ratio[b] (95% CI)	% Attribute to ED[c]
Aggressive Behaviour:					
Verbally fought	378	32	16	0.41 (0.33, 0.51)***	5
Physically fought	375	14	8	0.50 (0.38, 0.67)***	15
Mental and Physical Injury, Distress, or Harm:					
Acted in a way that resulted in me experiencing guilt	380	49	26	0.36 (0.30, 0.44)***	14
Acted in a way that resulted in me experiencing humiliation	377	46	30	0.51 (0.42, 0.60)***	16
Passed out	380	32	18	0.47 (0.38, 0.59)***	19
Physically hurt or injured	375	27	14	0.46 (0.36, 0.58)***	17
Required emergency medical treatment	379	3	1	0.24 (0.82, 0.73)*	25^
Antisocial Behaviour:					
Acted on a dare which could cause harm to myself and/or others	377	15	9	0.53 (0.40, 0.71)***	16
Asked to leave and/or kicked out of a drinking establishment	383	21	11	0.45 (0.34, 0.60)***	0
Vandalised	379	5	2	0.29 (0.13, 0.65)**	67^
Cautioned, restrained, charged, and/or fined by the police	379	4	2	0.37 (0.17, 0.78)*	33^

Note. [a] Indicates the percentage of participants who endorsed the event as present in an alcohol mixed with energy drink (AmED) session/alcohol session; [b] An odds ratio of 1 indicates the event was equiprobable in each session, > 1 indicates the event was more likely to occur in AmED sessions relative to alcohol sessions, and <1 indicates the event was less likely to occur in AmED sessions relative to alcohol sessions; [c] This percentage reflects the number of AmED users who had engaged in the risk behaviour in an AmED session and reported that they attributed 'most' or 'all' of their behaviour to ingesting energy drinks (EDs) with alcohol, compared to those who attribute 'none' or 'some' of their behaviour to co-ingestion; ^ indicates small sample size ($n \leq 10$); # indicates that the attribution item was not measured for this risk behaviour due to the sensitivity of the question; *p<.050; ** p<.010; ***p<.001.

4.5.4 AmED and Alcohol Physiological Outcomes

Physiological outcome analyses indicated several negative outcomes of AmED consumption potentially associated with EDs' stimulatory properties (Table 2). AmED users recorded six times higher odds of experiencing heart palpitations and four times higher odds of enduring sleep difficulties during AmED sessions relative to alcohol sessions. Heightened stimulation was also evident via significantly increased odds of tremors, general psychomotor agitation, jolt and crash episodes (a period of increased stimulation followed by a sharp, sudden drop in energy), and increased speech speed during AmED relative to alcohol sessions. However, AmED ingestion also appeared to be associated with some negation of alcohol-induced sedation, as the odds of experiencing nausea, slurred speech, and impairment of walking and vision were significantly less in AmED sessions relative to alcohol sessions.

4.5.5 AmED and Alcohol Psychological Outcomes

Similar to the physiological outcomes, psychological outcome analyses yielded differential outcomes of AmED ingestion relative to alcohol consumption (Table 3). The odds of experiencing stimulatory mood states were significantly higher, and sedation mood states were significantly lower, in AmED sessions relative to alcohol sessions. However, participants reported significantly higher odds of feeling 'on edge' and irritable, and significantly lower odds of feeling sociable and content, during AmED sessions compared to alcohol sessions. More extreme antisocial moods (i.e., aggression) evidenced equivalent odds across session type. Similarly, feelings of impulsivity and novelty-seeking were generally reported at a consistently high rate regardless of session type. However, AmED users did have significantly

lower odds of experiencing disinhibition in AmED sessions relative to alcohol sessions.

Table 2

Percentage (%) and Odds Ratio for Physiological Outcomes of Intoxication in AmED Sessions Relative to Alcohol Sessions

Physiological Outcome	***N***	**% Alcohol Session[a]**	**% AmED Session[a]**	**Odds Ratio[b] (95% CI)**
Headache	379	39	38	0.94 (0.80, 1.10)
Heart palpitation	377	6	27	5.79 (3.84, 8.73)***
Dizziness	381	35	34	0.93 (0.81, 1.07)
Tremors	379	10	22	2.48 (1.88, 3.27)***
Nausea	378	32	28	0.82 (0.69, 0.97)*
Vomiting	377	14	13	0.93 (0.74, 1.17)
Increased saliva	350	12	14	1.14 (0.93, 1.39)
Increased sweating	359	16	18	1.15 (0.97, 1.37)
Vision difficulty	369	20	17	0.85 (0.73, 0.99)*
Difficulty breathing	369	4	5	1.32 (0.90, 1.95)
Difficulty walking	376	34	29	0.78 (0.68, 0.90)**
Jolt and crash episode	373	15	22	1.64 (1.29, 2.08)***
Agitation	372	10	19	2.06 (1.54, 2.76)***
Hearing disturbance	375	11	13	1.17 (0.97, 1.41)
Slurred speech	379	31	24	0.68 (0.58, 0.80)***
Increased speed of speech	375	21	26	1.33 (1.11, 1.59)**
Inability to sleep	381	11	34	4.13 (3.08, 5.54)***

Note. [a] Indicates the percentage of participants who endorsed the event as present in an alcohol mixed with energy drink (AmED) session/alcohol session; [b] An odds ratio of 1 indicates the event was equiprobable in each session, > 1 indicates the event was more likely to occur in AmED sessions relative to alcohol sessions, and <1 indicates the event was less likely to occur in AmED sessions relative to alcohol sessions; 95% CI: 95% confidence interval; *p<.050, ** p<.010, ***p<.001.

Table 3

Percentage (%) and Odds Ratio for Psychological Outcomes of Intoxication in AmED Sessions Relative to Alcohol Sessions

Psychological Outcome	***N***	**% Alcohol Session[a]**	**% AmED Session[a]**	**Odds Ratio[b] (95% CI)**
Stimulatory Mood State:				
Alert	365	49	69	2.34 (1.94-2.84)***
Energetic	371	74	83	1.79 (1.42-2.26)***
Stimulated	368	62	70	1.42 (1.22-1.66)***
Active	369	77	80	1.16 (0.99-1.35)
Sedation Mood State:				
Confused	372	23	17	0.68 (0.57-0.80)***
Exhausted	373	31	16	0.43 (0.34-0.54)***
Sad	368	10	5	0.53 (0.38-0.74)***
Antisocial Mood State:				
On edge	370	9	15	1.73 (1.33-2.24)***
Irritable	372	9	12	1.30 (1.03-1.64)*
Annoyed	371	16	14	0.90 (0.73-1.12)
Aggressive	372	10	12	1.22 (0.95-1.57)
Contentment/Sociability Mood State:				
Calm	367	65	48	0.50 (0.42, 0.59)***
Carefree	372	82	77	0.73 (0.63, 0.84)***
Outgoing	372	88	85	0.77 (0.63, 0.95)*
Friendly	372	94	90	0.58 (0.44, 0.78)***
Sociable	373	94	91	0.67(0.51, 0.88)**
Impulsive Mood State:				
Daring	371	54	54	1.01 (0.93, 1.10)
Adventuresome	369	75	73	0.92 (0.81, 1.04)
Headstrong	364	62	61	0.96 (0.88, 1.03)
Impulsive	372	55	53	0.92 (0.83, 1.01)
Disinhibited	370	64	60	0.83 (0.75, 0.92)**

Note. [a] Indicates the percentage of participants who endorsed the event as present in an AmED session/alcohol session; [b] An odds ratio of 1 indicates the event was equally probable in each session, > 1 indicates the event was more likely to occur in AmED sessions relative to alcohol sessions, and <1 indicates the event was less likely to occur in AmED sessions relative to alcohol sessions; 95% CI: 95% confidence interval; *p<.050, ** p<.010, ***p<.001.

4.6 Discussion

The aim of the present study was to determine the subjective psychological, physiological, and behavioural risk-taking consequences of AmED and alcohol ingestion in a sample of AmED users recruited from the community. The results revealed that co-ingestion yielded a double-edged effect in regards to the physical and psychological manifestation of intoxication. In addition to demonstrating lower odds of physiological (e.g., nausea, walking and speech difficulties) and psychological (e.g., confusion, sadness) sedation side-effects, AmED users reported significantly higher odds of experiencing stimulatory mood states, such as increased energy and alertness. Surprisingly, while risk-taking outcomes were present during both session types, the odds of engaging in all assessed risk behaviours were significantly lower during AmED sessions relative to alcohol sessions. While a greater quantity of alcohol was typically consumed in AmED sessions, the difference in quantity was equivalent to approximately half a standard alcoholic drink. Additionally, participants reported significantly lower odds of experiencing disinhibition during AmED sessions. However, co-ingestion was also associated with several negative outcomes potentially related to over-stimulation, as AmED users had significantly higher odds of experiencing negative physiological (e.g., heart palpitations, agitation, tremors, sleep difficulties, jolt and crash episodes) and psychological (e.g., tension, irritability) outcomes.

The existing proposal of increased risk-taking post-AmED consumption was based on the premise that AmED may compromise assessment of intoxication, resulting in increased alcohol consumption and increased engagement in other risk-taking (Ferreira et al., 2006; Weldy, 2010). This hypothesis has gained preliminary support

from findings of equivalent impairment on objective measures, despite lower ratings of intoxication on some subjective measures following AmED consumption (Ferreira et al., 2006; Marczinski et al., 2011; Marczinski et al., 2012). However, participants in the current study also reported lower odds of experiencing disinhibition during AmED sessions relative to alcohol sessions. The current behavioural risk-taking outcomes contradict those of Thombs et al. (2010), who found that bar patrons who had consumed AmED were more likely to report an intention to drive intoxicated compared to those who had not consumed AmED. Thombs et al.'s (2010) research has the advantage of increased ecological validity due to the setting for testing. However, inferences regarding risk-taking by AmED users are limited as participants were reporting an intention which may not necessarily translate into action. The results of the current study are based on retrospective reporting of actual engagement in a range of behaviours which vary in type and level of risk. This element of the design may also explain the inconsistency between the present findings and those of Woolsey et al. (2010), who examined American university student athletes' expectancies regarding risk-taking outcomes of AmED and alcohol sessions. Further objective measurement of risk-taking via laboratory-based instruments across a range of dosages which may be consumed in 'real world' scenarios is necessary to explore this tentative hypothesis. Use of psychophysiological measurement techniques (i.e., electroencephalographic measurement) may also clarify the specific cognitive processes impacted by AmED ingestion relative to alcohol only.

However, the increased stimulation and alertness associated with co-ingestion may result in several negative outcomes. While current research now suggests that the performance-enhancing effects of EDs cannot be attributed solely to caffeine

(Marczinski et al., 2011; Scholey & Kennedy, 2004), the stimulation-related negative psychological and physiological side-effects reported during AmED sessions are in all likelihood a function of ED caffeine content. The increased odds of tension, irritability, tremors, agitation, heart palpitations, sleeping difficulties, and jolt and crash episodes reported by participants during AmED sessions are common side-effects of caffeine overconsumption (Reissig et al., 2009). This is not to say that the caffeine content of a standard ED will necessarily result in such side-effects. The average ED intake during AmED sessions was significantly higher than the Australian recommended daily intake (Food Standards Australia and New Zealand, 2009), with some users reporting consumption of 10 standard EDs per session (equivalent to 800mg caffeine). Investigation of AmED users' knowledge regarding caffeine intoxication side-effects, ED caffeine content, and ED recommended intake may elucidate whether this excess consumption is intentional or prompted by a lack of awareness. If the latter is true, then this may be an important focus of health education interventions.

The results of the present study should be interpreted with caution as the data were self-reported to maintain confidentiality and is thus subject to potential bias, particularly as no 'lie' questions were embedded within the survey to assess the consistency of responses. However, certain considerations were implemented to minimise this bias, including the use of a web-based survey to allow participants to complete the survey independently, collection of non-identifying information to assure anonymity, and entry of contact details for prize draw entry on a secure, independent webpage. An advantage of this study was recruitment beyond the university student population, in that data was also provided by a range of AmED

users outside of the university student drinking culture. However, we cannot assume the sample is fully representative of the community, as participants were self-selected in response to recruitment advertisements. Furthermore, examination of the demographic data indicates that the AmED sample primarily consisted of females in their early to middle twenties who had completed further post-secondary qualifications and were employed on a part- to full-time basis. Longitudinal studies on alcohol use trajectories suggest that a decline in alcohol use becomes apparent by the mid-twenties, when users are generally transitioning into adult roles (e.g., worker, parent, spouse) (Maggs & Schulenberg, 2004). Thus, the current study may have captured predominantly older AmED users in the midst of altering their general alcohol consumption practices. Closer examination of the sample age composition revealed that 28% were aged 18 to 20 years. Thus, whilst the current study provides a picture of AmED use by young Australian adults, more purposive sampling of individuals who have recently reached the legal drinking age limit (18 years in Australia) and who are undergoing the transition from high school to university or workforce may yield divergent findings. Additionally, there has been limited investigation of adolescent AmED use, despite evidence to suggest the primary ED user type may be shifting to a younger demographic. For example, the proportion of young females aged 14 to 17 among the ED user cohort increased from 9% in 2004 to 16% in 2006 (Levy & Tapsell, 2007). Thus, investigation of AmED use within this age group may be warranted, particularly in light of the later-life impact of alcohol consumption within this critical period (Grant et al., 2006).

In summary, co-ingestion of ED with alcohol appears to offer a reduction in the experience of sedation outcomes but amplification of adverse stimulation outcomes.

The lower odds of disinhibition and behavioural risk-taking in AmED sessions may be attributable to enhanced arousal post-ED consumption, consequently increasing attentional resources for information processing. However, overconsumption of EDs when co-ingesting may counteract any possible benefits of increased stimulation, with increased odds of negative physiological and psychological side-effects potentially related to caffeine intoxication.

4.7 References

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Chapter 5: Self-Reported Physiological and Psychological Side-Effects of an Acute Alcohol and Energy Drinks

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5.1 Preface

This chapter outlines the results from an experimental study (*Study 2*) regarding the self-reported physiological and psychological side-effects of an acute dose of AmED (relative to alcohol) in a controlled setting. This manuscript extended the methodology reported in *Chapter 4* by assessing similar outcomes using an experimental, as opposed to retrospective survey, methodology (*Question 4*). This design minimised the risk of recall bias, in that consumers self-reported outcomes during intoxication as opposed to retrospectively recalling experiences over multiple drinking sessions. Furthermore, participants in *Study 2* were identifying the effects of a fixed dose as opposed to reporting outcomes across several drinking periods with potentially variable intake. The results of this study, coupled with the outcomes reported in *Chapter 4*, illustrate the nature of the AmED intoxication experience in regards to the stimulation- and sedation-based outcomes experienced by consumers.

5.2 Abstract

Background: There have been repeated calls from health professionals and policy-makers to clarify the side-effects of the increasingly popular consumption trend of alcohol mixed with energy drinks (AmED). There is a dearth of research assessing the differential effects of AmED relative to alcohol by comparing self-reported psychological and physiological outcomes whilst under the influence of these substances. The aim of the present study was to examine the acute effects of a moderate alcohol and low energy drink (ED) dose on self-reported psychological and physiological outcomes.

Method: Using a single-blind, placebo-controlled, crossover design, 28 adults completed four sessions where they were administered: (i) 0.50g/kg alcohol, (ii) 3.57mL/kg ED, (iii) AmED, and (iv) placebo. Participants independently completed the Profile of Mood States and a Somatic Symptom Scale at baseline and 30 and 125 minutes after beverage administration.

Results: Breath alcohol concentration peaked at .068% and .067% in the alcohol and AmED conditions respectively. There were no interactive alcohol and ED effects on self-reported psychological outcomes. Treatment effects for physiological outcomes generally only related to alcohol or ED administration, with the exception of decreased heart palpitation ratings following AmED relative to alcohol. Decreased muscular tension ratings were evident when the two constituents were consumed separately relative to placebo.

Conclusions: The results provide evidence of only limited subjective changes in physiological and psychological state after consuming AmED relative to alcohol. The majority of effects arose from independent effects of alcohol or ED, rather than being modified by their interaction. However, research extending into higher dosage

domains is required to increase outcome generalisability for consumers in the night-time economy.

5.3 Introduction

Consumption of alcohol mixed with energy drinks (AmED) is an increasingly popular trend amongst adolescents and young adults, with prevalence estimates of recent AmED use among college student samples ranging between 23% and 48% (Brache & Stockwell, 2011; Oteri et al., 2007). Recent publications outlining increases in energy drink (ED)-related emergency department visits (Substance Abuse and Mental Health Service Administration, 2011) and poison information centre calls (Gunja & Brown, 2012) have heightened concerns regarding the health effects of EDs and AmED. Several national bodies have released public statements highlighting the potential additional health harms of AmED consumption (Australian Medical Association, January, 2013; United States Food and Drug Administration, November, 2010). However, there is a dearth of research directly comparing the pharmacological effects of AmED versus alcohol on perceived physiological and psychological outcomes.

Only one recent community survey by Peacock et al. (2012) has directly compared the subjective side-effects of AmED and alcohol consumption. This comparison revealed that AmED consumers self-reported significantly greater odds of experiencing subjective physiological and psychological side-effects related to over-stimulation (i.e., heart palpitations, sleeping difficulties, agitation, tremors, increased speech speed, jolt and crash episodes, irritability and tension), and lower odds of side-effects related to sedation (i.e., nausea, slurred speech, and walking and vision difficulties) when ingesting alcohol with ED relative to without ED (Peacock et al., 2012). However, recall bias may have been an issue, as reporting required retrospective recall of side-effects in the preceding six months.

Assessment of acute subjective side-effects in a controlled environment rules out such biases. However, the few experimental studies conducted to date have generally focused on overall stimulation and sedation ratings (Marczinski et al., 2011; Marczinski et al., 2012, 2013; Peacock et al., 2013c). Only Alford et al. (2012) have assessed a range of psychological outcomes, generally finding no significant change between ratings after ingestion of alcohol (0.046% and 0.087% BrAC) alone and in combination with ED. However, the researchers acknowledge that the between-subjects design and small sample size may have contributed to the absence of significant findings. Ferreira et al. (2006) have directly assessed subjective physiological outcomes, demonstrating lower ratings of dry mouth and alterations of motor coordination 120 minutes following co-ingestion of 0.65g/kg and 1.0g/kg alcohol with 3.57mL/kg ED relative to these doses without ED. In contrast with AmED consumers' retrospective self-report of AmED experiences (Peacock et al., 2012), indices of over-stimulation (e.g., tremor, tachycardia) did not differ between AmED and alcohol conditions.

The dearth of research assessing subjective acute physiological and psychological outcomes of alcohol and ED consumption limits the available evidence for an informed response to the international rise in AmED use and associated harms. Following from repeated calls from researchers and health professionals, the present study was undertaken to determine the effects of a moderate alcohol and low ED dose on subjective physiological and psychological outcomes, specifically the Profile of Mood States (McNair et al., 1979) and a Somatic Symptom Scale derived from Ferreira et al. (2006).

5.4 Method

5.4.1 Participants

Twenty-eight adults (14 males; *M*=19.5, *SD*=1.8, range 18-25 years) participated in a single-blind, placebo-controlled, crossover study. The sample consisted of regular caffeine (5-28 caffeinated products in the preceding week), alcohol (minimum of two standard drinks in the preceding fortnight), and ED (minimum of one standard 250mL ED in the preceding month; maximum consumption of one standard 250mL ED per day in the preceding month) consumers who self-reported no: (i) significant physical or psychiatric history, (ii) current pregnancy or lactation, (iii) regular current tobacco, medication, or illicit drug use. Volunteers who scored 16 or higher on the Alcohol Use Disorders Identification Test (AUDIT; Babor, Higgins-Biddle, Saunders, & Monteiro, 2001) were excluded.

The study protocol was approved by the Human Research Ethics Committee Tasmania Network and volunteers provided informed consent. Participants were informed they may receive alcohol (maximum of six standard alcoholic drinks) and ED (maximum of three standard 250mL EDs). Recruitment occurred via public advertisements at the University of Tasmania. Participants were reimbursed 120 AUD.

5.4.2 Measures

The Profile of Mood States (POMS; McNair et al., 1979) was used to assess perceived current psychological state. Participants rated how accurately 65 adjectives described their current mood on a 5-point Likert scale ranging from 0 ‘not at all’ to 4

'extremely'. Total Mood Disturbance and Tension-Anxiety, Depression-Dejection, Confusion-Bewilderment, Anger-Hostility, Fatigue-Inertia, and Vigour-Activity subscale scores were calculated, with higher scores indicating greater perceived disturbance.

A Somatic Symptom Scale (SSS), consisting of 20 100-mm visual analogue scales (0mm anchor designated 'not at all', 100mm anchor designated 'extremely'), was used to assess current perceived physiological state (e.g., 'headache', 'dizziness'); items were derived from previous AmED research by Ferreira et al. (2006). Item scores ranged from 0 to 100, with higher scores indicating greater intensity of the physiological outcome.

A Beverage Rating Scale (BRS; Fillmore & Vogel-Sprott, 2000) was used to assess perceived alcohol and ED intake and confirm successful placebo manipulation. Participants reported the perceived number of alcoholic drinks (each drink 4.8% alcohol/volume or 1.4 standard drinks; range 0-10 drinks increasing in 0.5 increments) and standard 250mL EDs (range 0-3 increasing in 0.5 increments) administered.

5.4.3 Treatment Conditions

Participants were randomly assigned a counterbalanced treatment order: (i) 0.50g/kg vodka (37.5% alcohol/volume Smirnoff Red Label®), (ii) 3.57ml/kg Red Bull® ED (Red Bull GmbH), (iii) AmED, and (iv) placebo. The alcohol dose (decreased to 85% for females) was chosen to yield a peak BrAC of 0.05%, the Australian legal limit for driving, while the ED dose was equivalent to one 250mL ED per 70kg

person, reflecting the dosing protocol adopted by Ferreira et al. (2006). The specific beverages (vodka and Red Bull®) were chosen based on endorsement in a recent Australian survey study as the most popular AmED mixers (Peacock et al., 2012). The placebo alcohol dose was achieved by floating 5ml vodka on each beverage portion, with a light alcohol mist sprayed on the inner container (Marczinski & Fillmore, 2006). The placebo ED dose was 3.57mL/kg Red Bull® minus caffeine, taurine, glucuronolactone, inositol, and B vitamin complex content; sugar content was identical for active and placebo beverages (27g/250mL). Data collectors, participants, and data analysts were blind to ED administration; only participants and data analysts were blind to alcohol administration.

5.4.4 Procedure

Participants attended a 90-minute familiarisation session where they completed screening measures, were weighed for substance administration purposes, and familiarised with the experimental procedure. Participants then attended four 180-minute experimental sessions conducted between 0930 and 1900 and separated by a minimum of two and maximum of 10 days. Participants were required to fast for four hours (excluding consumption of a standard breakfast bar 90 minutes prior to session commencement) and abstain from caffeine for eight hours, from alcohol and prescription medication for 24 hours prior to each session, and from illicit drugs throughout the duration of participation. Following completion of baseline POMS and SSS measures, participants were administered the beverage in two portions served in opaque lidded cups, consuming each portion within a 5-minute period. Post-drink administration of the POMS and SSS occurred 30 minutes and 125 minutes after initiation of beverage consumption, with the BRS administered at the

latter time point. BrAC was also tested at these points using an Alcolizer HH-2 breathalyser. All self-report data were collected via computerised survey software to minimise experimenter bias. It should be noted that participants completed several cognitive tasks, and electroencephalographic data were collected, in the interval between the post-drink assessments (partial results detailed in Peacock et al., 2013c). At the conclusion of the session, participants received a detoxification meal and remained at leisure in the laboratory until recording two BrAC measurements of .030% or less over 15 minutes.

5.4.5 Data Analysis

Two participants had missing POMS and SSS data (N=26) and one participant had missing BRS data (N=27) due to technical malfunction. Data were analysed in IBM SPSS Statistics 19. POMS subscale and Total Mood Disturbance scores and SSS item ratings were calculated as the change from baseline at each time point (30 and 125 minutes post-beverage administration) and analysed using 2 (Alcohol: Active, Placebo) x 2 (ED: Active, Placebo) ANOVAs, with Bonferroni-adjusted follow-up paired sample *t*-tests. Effect size was calculated using Hedges' g (Hedges, 1981). To enhance clarity, effects of moderate magnitude ($g \geq 0.5$) are discussed where $p < .100$.

5.5 Results

5.5.1 Sample Characteristics

Participants typically reported above-average intelligence, low psychological distress, and a normal body mass index (Table 1). Median AUDIT scores of 9 and 10 have been reported in community samples of young Australian males and females respectively (Bowring, Gouillou, Hellard, & Dietze, 2013); the mean AUDIT score

for the present sample was 8.1 (*SD*=3.0, range 3.0-14.0). Participants were typically moderate caffeine consumers who ingested EDs on a monthly or less basis (29%) or on a fortnightly to weekly basis (32%); more frequent use was only reported by 39% of the sample. Participants generally reported that typical ED intake fell within the Australian recommended maximum daily intake guidelines (i.e., maximum of two standard 250mL EDs; 80mg caffeine per standard serve).

Table 1

Sample Characteristics (Standard Deviation in Parentheses; N=28)

Outcome[a]	**Mean (*SD*)**	**Range**
Psychological distress (K10)	15.8 (3.3)	12.0-26.0
Intellectual functioning (WTAR)	106.4 (10.3)	87.0-126.0
Weight (kg)	73.0 (14.4)	53.0-109.8
Body mass index	23.6 (3.0)	18.3-30.0
TLFB Alcohol Use (past month):		
Days any alcohol	7.5 (5.2)	2.0-23.0
Days exceed NHMRC lifetime low-risk guideline	4.4 (2.6)	0.0-10.0
Days exceed NHMRC session low-risk guideline	2.7 (2.3)	0.0-9.0
Average standard alcoholic drinks per drinking day	5.2 (3.2)	1.3-14.9
Maximum standard alcoholic drinks per drinking day	9.6 (5.1)	1.9-22.0
Caffeine/Energy Drink Use:		
Average daily caffeine intake (mg)	236.1 (130.8)	70.4-556.7
Average standard EDs (past month)	1.3 (0.6)	1.0-3.0
Maximum standard ED (past month)	2.4 (1.3)	1.0-6.0

Note. [a] Kessler Psychological Distress Scale (K10; Kessler et al., 2002) score range is 10-50, with scores ≥ 30 indicative of a moderate to severe psychological distress; Wechsler Test of Adult Reading (WTAR) standardised score is 100, with higher scores indicative of higher levels of pre-morbid intellectual functioning; body mass index scores between 17 and 29.9 indicate mild-thinness to pre-obese body mass; the Timeline Follow Back (TLFB; Sobell & Sobell, 1992) reflects retrospective self-reported alcohol consumption in the preceding month; National Health and Medical Research Council (NHMRC, 2009) lifetime low risk guideline is a maximum of two standard alcoholic drinks on any day; NHMRC session low risk guideline is a maximum of four standard alcoholic drinks on any day; the Caffeine Energy Drink Use Questionnaire standardised an energy drink (ED) unit as 250ml ED containing approximately 80mg caffeine.

Table 2

Treatment Condition Baseline Ratings and Change from Baseline Ratings at 30 Minutes and 125 Minutes Post-Beverage Administration for POMS Subscales and SSS Scores (Standard Deviation in Parentheses, N=26)

Outcome	Baseline				30 minutes					125 minutes				
	Placebo	***ED***	***Alcohol***	***AmED***	***Placebo***	***ED***	***Alcohol***	***AmED***	***Effect[a]***	***Placebo***	***ED***	***Alcohol***	***AmED***	***Effect[a]***
Self-Reported Psychological Outcomes (POMS):														
Tension-Anxiety	4.1 (3.1)	3.8 (2.9)	3.2 (2.6)	4.2 (3.7)	0.0 (3.3)	-0.7 (1.8)	-0.7 (2.9)	-0.6 (3.0)		-0.4 (2.5)	-0.7 (2.5)	1.0 (2.4)	-0.4 (3.1)	A~ E*
Depression-Dejection#	1.6 (3.7)	0.7 (1.3)	0.4 (1.1)	1.2 (2.7)	*0.4 (1.0)*	*0.6 (0.9)*	*0.5 (0.6)*	*0.5 (0.8)*		*0.3 (0.8)*	*0.4 (0.5)*	*0.8 (1.4)*	*1.2 (1.9)*	*A~*
Confusion-Bewilderment	4.7 (3.0)	4.0 (1.9)	3.7 (1.8)	4.1 (2.4)	-0.5 (1.5)	0.2 (1.5)	1.2 (2.5)	1.0 (3.6)	A*	0.3 (2.3)	-0.5 (1.9)	1.0 (2.6)	1.1 (2.5)	A**
Total Mood Disturbance	16.9 (13.7)	13.0 (8.7)	13.9 (7.8)	14.5 (9.5)	-4.7 (9.9)	-1.5 (10.5)	-3.7 (9.4)	3.4 (7.6)		-0.9 (14.4)	1.4 (9.4)	4.7 (14.1)	2.6 (11.6)	A*
Self-Reported Physiological Outcomes (SSS):														
Heart Palpitations	1.1 (3.9)	0.9 (4.3)	3.0 (11.0)	1.6 (5.4)	1.9 (4.9)	0.6 (3.2)	-2.2 (10.3)	1.8 (4.6)	AxED~	-0.2 (3.0)	0.9 (4.4)	-2.7 (11.1)	0.4 (5.5)	E~
Dizziness	3.1 (6.5)	3.8 (9.0)	4.4 (12.9)	3.4 (6.5)	-0.1 (3.4)	-1.4 (7.9)	12.5 (17.6)	14.3 (19.9)	A**	-1.7 (5.2)	-0.4 (9.8)	6.0 (12.6)	8.0 (16.4)	A*
Tremors	1.2 (4.5)	1.4 (4.0)	2.3 (10.2)	1.4 (5.1)	1.7 (4.2)	0.3 (2.1)	1.8 (9.9)	0.8 (4.9)		0.2 (2.1)	-1.1 (3.6)	-0.2 (1.0)	-0.2 (2.4)	AxED~
Increased Saliva	1.6 (5.0)	3.2 (11.0)	4.2 (13.0)	4.2 (11.1)	5.1 (11.3)	4.0 (12.8)	8.4 (18.9)	9.9 (23.6)	A~	2.1 (6.8)	0.2 (13.9)	1.2 (7.4)	5.4 (18.1)	
Vision Difficulty	3.3 (11.3)	5.0 (13.4)	2.7 (9.4)	4.5 (10.8)	-0.4 (5.5)	0.6 (12.4)	11.2 (18.9)	13.1 (15.9)	A**	4.9 (18.0)	0.6 (15.9)	6.4 (15.0)	4.2 (10.9)	

Table 2 Continued

Outcome	Baseline				30 minutes					125 minutes				
	Placebo	***ED***	***Alcohol***	***AmED***	***Placebo***	***ED***	***Alcohol***	***AmED***	***Effect[a]***	***Placebo***	***ED***	***Alcohol***	***AmED***	***Effect[a]***
Self-Reported Physiological Outcomes (SSS) Continued:														
Walking Difficulty	3.4 (12.1)	6.0 (17.2)	4.2 (12.5)	2.7 (10.9)	-0.9 (6.6)	-1.2 (15.9)	8.6 (15.3)	15.1 (22.0)	A**	-1.0 (5.9)	-2.0 (15.8)	5.6 (11.5)	5.6 (13.1)	A*
Hearing Difficulty	0.6 (2.8)	5.0 (13.8)	2.2 (10.0)	3.2 (11.9)	0.0 (1.3)	-3.5 (11.3)	0.4 (2.0)	1.6 (6.9)	A* AxED~	0.6 (2.5)	-3.4 (13.4)	1.3 (18.5)	-1.9 (11.3)	
Slurred Speech	2.5 (10.1)	5.9 (15.2)	5.9 (17.2)	5.1 (15.7)	1.5 (5.8)	-1.5 (12.8)	8.1 (14.0)	12.7 (17.5)	A**	2.2 (9.5)	-1.6 (12.8)	5.6 (12.4)	5.5 (13.0)	A*
Fatigue	13.8 (20.1)	16.1 (20.5)	16.5 (24.1)	11.5 (16.7)	3.0 (13.6)	-4.7 (17.4)	-4.8 (20.0)	2.4 (16.3)		8.2 (30.6)	2.3 (22.4)	13.0 (25.0)	15.5 (22.9)	A~
Physical Weakness	8.2 (16.8)	8.4 (17.0)	9.7 (19.4)	6.6 (15.7)	-1.5 (7.5)	-1.4 (7.8)	2.5 (9.3)	2.4 (10.6)	A~	2.3 (18.2)	-0.7 (10.6)	3.8 (14.9)	6.7 (14.1)	A~
Muscular Tension	4.6 (9.7)	10.2 (17.9)	8.4 (20.3)	8.9 (20.0)	1.0 (7.0)	-6.1 (15.3)	-6.5 (18.8)	-3.1 (16.7)	AxED*	0.7 (6.1)	-4.4 (12.2)	-5.1 (19.8)	-1.0 (14.1)	AxED~
Alteration in Motor Coordination	6.5 (13.9)	6.4 (15.6)	5.1 (15.8)	8.7 (19.3)	0.6 (7.5)	0.3 (14.3)	17.5 (23.1)	19.0 (20.2)	A**	3.1 (14.4)	3.2 (23.4)	11.7 (21.4)	11.0 (16.3)	A*

Note. [a] 'A' indicates a significant main effect of Alcohol, 'E' indicates a significant main effect of ED, and 'AxED' indicates a significant Alcohol x ED interaction; ~p<.100, * p<.050, **p<.001. POMS score ranges were: Total Mood Disturbance: -32 to 200; Tension-Anxiety: 0-36; Depression-Dejection: 0-60; Confusion-Bewilderment: 0-28; Anger-Hostility: 0-48; Fatigue-Inertia: 0-28; and Vigour-Activity: 0-32. Higher POMS subscale and total change score indicate greater mood disturbance relative to baseline; mean scores for Anger-Hostility, Fatigue-Inertia, and Vigour-Activity are not reported due to an absence of treatment effects. SSS item score range is 0-100, with higher change scores indicating greater intensity of the outcome relative to baseline; mean ratings for headache, nausea, sweating, breathing difficulties and overall wellbeing are not reported due to an absence of treatment effects. # Note that while all outcomes were analysed using 2 (Alcohol: Active, Placebo) x 2 (ED: Active, Placebo) ANOVAs, baseline differences were detected for Depression-Dejection, meaning that the raw scores at 30 and 125 minutes for this outcome were analysed using Mixed Models for Repeated Measures with Baseline Score as a covariate; the baseline-adjusted mean scores are presented in this table. ED: energy drink; AmED: alcohol mixed with energy drink; POMS: Profile of Mood States; SSS: Somatic Symptom Scale.

5.5.2 Breath Alcohol Concentration

There was no significant difference in mean BrAC for alcohol and AmED conditions at 30 minutes (*M*=.068, *SD*=.019 and *M*=.067, *SD*=.018), *t*(28)=.30, *p*=.767, *g*<0.01, and 125 minutes (*M*=.039, *SD*=.009 and *M*=.040, *SD*=.007), *t*(28)=0.73, *p*=.474, *g*=0.11, after beverage administration.

5.5.3 Subjective Psychological Outcomes

The main effect of Alcohol (*p*s>.122), Alcohol x ED interaction (*p*s>.202), and main effect of ED (*p*s>.159) were non-significant for POMS Anger-Hostility, Fatigue-Inertia, and Vigour-Activity change scores.

Significant treatment effects for self-reported psychological outcomes are displayed in Table 2. In regards to Total Mood Disturbance, the only treatment effect was a significant main effect of Alcohol recorded at 125 minutes, *F*(1,25)=4.716, *p*=.040, *g*=0.45, with increased disturbance in active relative to placebo alcohol conditions. There was a main effect of Alcohol for Confusion-Bewilderment change scores at 30 minutes, *F*(1,25)=6.601, *p*=.011, *g*=0.73, and 125 minutes, *F*(1,25)=6.793, *p*=.015, *g*=0.63, with increased ratings in active relative to placebo alcohol conditions. No other significant treatment effects were recorded.

The main effect of Alcohol also trended towards significance for Tension-Anxiety change scores but only at 125 minutes, *F*(1,25)=4.216, *p*=.051, *g*=0.43, with increased Tension-Anxiety scores in active relative to placebo alcohol conditions. A significant main effect of ED was also evident at 125 minutes only for Tension-Anxiety, *F*(1,25)=5.649, *p*=.025, *g*=0.40, with decreased Tension-Anxiety in active

relative to placebo ED conditions. There was no significant interaction at any time point.

Depression-Dejection was the only scale to show a difference in ratings between treatment conditions at baseline, with a significant Alcohol x ED interaction (p=.045). Consequently, analysis of the raw data for this outcome comprised Mixed Models for Repeated Measures regression with a diagonal covariance structure. The basic model tested included Alcohol (Active, Placebo), ED (Active, Placebo) and Alcohol x ED as fixed factors, with Subject as a random factor and baseline Depression-Dejection raw scores as the covariate. While no significant treatment effects were evident at 30 minutes, there was a significant main effect of Alcohol at 125 minutes, $F(1,7)=7.212$, p=.009, g=0.99, with a large magnitude increase in ratings in the active relative to placebo alcohol conditions.

5.5.4 Subjective Physiological Outcomes

The main effect of Alcohol (ps>.147), Alcohol x ED interaction (ps>.105), and main effect of ED (ps>.136) were non-significant for SSS change ratings of headache, nausea, sweating, breathing difficulties, agitation, and overall wellbeing.

Treatment effects for self-reported physiological outcomes are displayed in Table 2. There was a significant main effect of Alcohol at 30 and 125 minutes post-beverage administration for dizziness (30 minutes: $F(1,25)=20.898$, p<.001, g=1.16; 125 minutes: $F(1,25)=9.405$, p=.005, g=0.90), walking difficulty (30 minutes: $F(1,25)=20.205$, p<.001, g=1.00; 125 minutes: $F(1,25)=10.534$, p=.003, g=0.69), slurred speech (30 minutes: $F(1,25)=19.544$, p<.001, g=1.09; 125 minutes:

F(1,25)=5.724, *p*=.025, *g*=0.57) and alterations in motor coordination (30 minutes: *F*(1,25)=32.808, *p*<.001, *g*=0.55; 125 minutes: *F*(1,25)=4.440, *p*=.045, *g*=1.34), with increased ratings in active relative to placebo alcohol conditions. There was also a significant main effect of Alcohol at 30 minutes only for vision difficulty, *F*(1,25)=21.578, *p*<.001, *g*=1.06, and a trend towards a significant main effect of Alcohol for salivation at 30 minutes, *F*(125)=3.227, *p*=.085, *g*=.0.39, for fatigue at 125 minutes, *F*(1,25)=3.421, *p*=.076, *g*=0.46, and for physical weakness at both time points (30 minutes: *F*(1,25)=4.225, *p*=.050, *g*=0.59; 125 minutes: *F*(1,25)=3.054, *p*=.093, *g*=0.43), with increased ratings in active relative to placebo alcohol conditions. There were no other significant treatment effects for these variables.

While a main effect of Alcohol was evident at 30 minutes for hearing difficulty, *F*(1,25)=5.038, *p*=.034, *g*=0.55, with a moderate magnitude decrease in ratings in placebo relative to active alcohol conditions at 30 minutes, a trend toward a significant Alcohol x ED interaction was also observed at 30 minutes, *F*(1,25)=3.901, *p*=.059. Follow-up comparisons showed small-to-moderate magnitude decreases in hearing disturbance ratings which trended towards significance in the ED condition relative to alcohol (*p*=.096, *g*=0.47) and AmED (*p*=.043, *g*=0.54) conditions; no other comparisons neared significance (*p*s>.116), with no significant difference in ratings between alcohol and AmED conditions (*p*=.391, *g*=0.24).

A trend towards a significant Alcohol x ED interaction was also evident at 30 minutes only for heart palpitation ratings, *F*(1,25)=3.453, *p*=.075; follow-up comparisons showed a moderate magnitude decrease in ratings which trended

towards significance in the alcohol relative to AmED (p=.100, g=0.50) and placebo (p=.080, g=0.51) conditions; no other comparisons neared significance (ps>.100). There was also a trend towards a significant main effect of ED at 125 minutes post-ingestion only, F(1,25)=3.561, p=.071, g=0.48, with a small magnitude increase in heart palpitations ratings in active compared to placebo ED conditions.

Similarly, a significant Alcohol x ED interaction was observed at 30 minutes only for muscular tension, F(1,25)=8.052, p=.009, with moderate magnitude decreases in muscular tension ratings in the ED (p=.015, g=0.60) and alcohol (p=.065, g=0.53) conditions relative to the placebo condition; no other comparisons neared significance (ps>.179), with no significant difference in ratings in the AmED and alcohol conditions (p=.235, g=0.19). The interaction also trended towards significance at 125 minutes, F(1,25)=3.276, p=.082, with a moderate magnitude decrease in ratings in the ED condition relative to the placebo condition (p=.022, g=0.53); no other comparisons neared significance (ps>.229), with no difference in ratings in the AmED and alcohol conditions (p=.403, g=0.24). A trend towards a significant Alcohol x ED interaction was also evident at 125 minutes only for tremor ratings, F(1,25)=3.410, p=.077, with decreased tremor ratings which trended towards significance in the ED relative to placebo condition (p=.080, g=0.43) but no difference between AmED and alcohol conditions (p=1.00, g<0.001).

5.5.5 Treatment Manipulation

For the BRS, participants reported greater perceived alcohol intake (1.4 standard drinks per unit) in active (M=2.9, SD=1.0) relative to placebo (M=0.50, SD=0.49) alcohol conditions, F(1,26)=152.164, p<.001, g=3.13. There was a small increase in

perceived alcohol intake which trended towards significance in active ED (*M*=1.8, *SD*=0.8) relative to placebo (*M*=1.6, *SD*=0.5) ED conditions, $F(1, 26)=4.062$, $p=.054$. There was no significant Alcohol x ED interaction ($p=.532$), with no significant difference in perceived alcohol intake in alcohol and AmED conditions ($p=.509$, $g=0.12$).

There was no significant main effect of ED ($p=.142$, $g=0.25$), main effect of Alcohol ($p=.946$, $g=0.02$), or Alcohol x ED interaction ($p=.958$) for BRS perceived ED intake. Average perceived ED intake in active and placebo ED conditions was 1.0 (*SD*=0.5) and 1.2 (*SD*=0.6) standard 250mL EDs respectively, with no significant difference in perceived intake in alcohol and AmED conditions ($p=.568$, $g=0.14$).

5.6 Discussion

There were no interactive effects of alcohol and ED on self-reported psychological outcomes. In general, alcohol consumption increased perceived confusion and total mood disturbance and ED consumption decreased perceived tension. There were no treatment effects for fatigue or vigour, despite previous AmED research showing increased ratings of drowsiness following alcohol ingestion (0.081%-0.094% BrAC) (Alford et al., 2012) and a trend towards decreased ratings of mental fatigue after consuming EDs (3.57mL/kg) (Marczinski et al., 2011).

Similarly, the majority of changes in perceived physiological state arose from the independent effects of alcohol or ED, rather than being modified by their interaction. Heart palpitations are a commonly reported outcome of ED and AmED consumption (S. C. Jones et al., 2012; Malinauskas et al., 2007; Peacock et al., 2012). However,

this outcome tended to show decreased ratings at 30 minutes after AmED relative to alcohol administration. ED and alcohol consumption tended to decrease muscular tension ratings, but only when the two constituents were ingested independently. Participants also tended to report lower tremor ratings when ED was ingested independent of alcohol relative to placebo.

In contrast with Ferreira et al. (2006), there was no interactive effect of AmED on perception of salivation and motor coordination. Indeed, the majority of perceived treatment effects were attributable to alcohol administration. With the exception of a trend towards ED-induced increased heart palpitation ratings, there were generally no significant effects of ED administration. While the ED dose in the present study matches that administered in past research (Alford et al., 2012; Ferreira et al., 2006; Marczinski et al., 2011; Marczinski et al., 2012), the discrepancy in intake under experimental conditions and in real-life AmED drinking sessions should be noted. An Australian community survey showed that AmED consumers typically ingested 2.4 standard 250mL EDs and 7.1 standard alcoholic drinks during AmED drinking sessions (Peacock et al., 2012), while approximately one standard 250mL ED and 3.5 standard alcoholic drinks (per 70kg person) were administered in the present study. The general absence of interactive alcohol and ED effects at these doses suggests that further research is required extending into these higher dosage domains to increase ecological validity and provide guidance at a policy level.

The target sample size of 24 was based on a prior power analysis yielding a moderate effect size (Cohen's *f*=.30), with the view that effect sizes smaller than this magnitude would be unlikely to have any practically meaningful effects. The final

sample for the study was 28, indicating that the study was sufficiently powered to detect meaningful effects (post-hoc estimated at Cohen's f>0.275 for power=0.80, α=0.05). Single-blind alcohol administration introduced possible experimenter bias, however systematic data collection procedures were implemented, data processing and analysis was blind, ED placebo manipulation was successful, and alcohol intake estimates did not differ significantly for AmED and alcohol conditions. While it is standard practice to require abstinence from the treatment prior to participation, reversal of adverse caffeine withdrawal effects may have contributed to outcomes (James & Keane, 2007). As session times varied for participants and caffeine abstinence was required for 8 hours, state of withdrawal may have differed across sessions and between participants. Future research should involve a single set time for sessions or a longer phase of caffeine abstinence to control for withdrawal reversal.

Despite these shortcomings, the present study has strengthened the evidence base regarding perceived AmED side-effects, generally revealing no interactive effects relative to the independent effect of the two constituents. These results suggest that changes in subjective physiological and psychological state after combining alcohol with an ED dose which falls below the Australian recommended maximum daily intake guidelines typically reflect the general effects of the two constituents rather than additive interactive effects of co-ingestion. However, AmED research needs to extend into higher dosage domains to increase the generalisability of outcomes for consumers.

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Chapter 6: The Impact of a Moderate Alcohol and Energy Drink Dose on Objectively Measured Risk-Taking Outcomes

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6.1 Preface

This chapter outlines the results from an experimental study (*Study 2*) which assessed the effects of an acute alcohol and ED dose on behavioural risk-taking. To date, this is the first published study to objectively measure risk-taking behaviour after consumption of alcohol with and without ED. In *Chapter 4* it was reported that, in contrast with predictions, an Australian community-based convenience sample of AmED consumers retrospectively self-reported lower odds of behavioural risk-taking after AmED relative to alcohol. This study was undertaken to determine whether the same pattern of results were evident after participants ingested a single dose of alcohol with or without ED in a controlled laboratory-based setting (*Question 5.1*), to clarify whether the addition of ED to alcohol caused an appreciable increase in risk-taking (as theorised) or a decrease in risk-taking (as reported in the *Chapter 4*). The results of this study, coupled with the outcomes reported in *Chapter 4*, indicate whether there may be an additional level of risk for consumers as a consequence of AmED intake. These outcomes provide an evidence base upon which to make decisions regarding the development and implementation of policy approaches specific to AmED.

6.2 Abstract

Background: It has been argued that consuming alcohol mixed with energy drinks (AmED) causes a subjective underestimation of intoxication and an increased level of risk-taking behaviour. To date, however, there is mixed support for AmED-induced reductions in perceived intoxication, and no objective assessment of risk-taking following AmED consumption. Consequently, the present study aimed to determine the effect of alcohol and energy drink (ED) consumption on subjective measures of intoxication and objective measures of risk-taking.

Method: Using a placebo-controlled, single-blind, crossover design, participants (*N*=28) attended four sessions in which they were administered, in counterbalanced order: 0.5g/kg alcohol, 3.57ml/kg ED, AmED, and a placebo beverage. Participants completed the Biphasic Alcohol Effects Scale and a Subjective Effects Scale at baseline and 30 and 125 minutes post-beverage administration; risk-taking was measured using the Balloon Analogue Risk-Task (BART).

Results: Participants reported greater subjective intoxication, impairment, and sedation after active relative to placebo alcohol consumption, with no interactive AmED effects. However, a significant moderate magnitude increase in stimulation ratings was observed in the AmED relative to alcohol, ED, and placebo conditions. There was no independent effect of alcohol, or interactive effect with ED, on the BART. A significant, yet small magnitude, increase in risk-taking was evident in active relative to placebo ED conditions.

Conclusions: The interactive effect of AmED appears restricted to perceived stimulation, with alcohol-induced increases in subjective intoxication occurring regardless of presence or absence of ED. Engagement in risk-taking behaviour was only increased by ED consumption however this effect was of small magnitude; at

these doses, alcohol consumption, with or without EDs, did not appreciably increase risk-taking. Further research assessing the dose-dependent effects of AmED on objectively measured risk-taking behaviour could clarify whether the ED effect increases with higher doses and whether an interactive effect is detected at higher alcohol doses.

6.3 Introduction

There is increasing concern as to the impact of consuming alcohol mixed with energy drinks (AmED) on perceived and actual intoxication. Few studies have examined the effect of AmED relative to alcohol on subjective intoxication outcomes in a laboratory-based setting. Initial research revealed reduced ratings of motor coordination and dry mouth after AmED relative to alcohol consumption (Ferreira et al., 2006). However, ratings of other subjective outcomes (e.g., 'tiredness', 'dizziness') typically evident at the recorded peak breath alcohol concentrations (.097 g/dL to .099g/dL) did not differ significantly for AmED and alcohol conditions. Later research has also produced mixed findings, with several studies showing reduced ratings on select indices argued to index intoxication (i.e., 'stimulation' and 'mental fatigue') post-AmED consumption (Marczinski et al., 2011; Marczinski et al., 2012), while others have revealed similar intoxication ratings across subjective measures for AmED and alcohol conditions (Alford et al., 2012).

Despite these disparate findings, several researchers (Arria & O'Brien, 2011; Weldy, 2010) have argued that AmED-induced underestimation of intoxication results in an increased likelihood of risk-taking behaviour. The majority of research regarding AmED consumption and risk-taking has focused on comparison of alcohol and AmED consumers. AmED consumers report greater typical alcohol intake, maximum alcohol intake, number of days intoxicated, and number of heavy episodic drinking days relative to non-AmED consumers (Brache & Stockwell, 2011; O'Brien et al., 2008; Woolsey et al., 2010) and the odds of AmED use by hazardous drinkers is four times higher relative to non-hazardous drinkers (L. Berger et al., 2011). A

field study in an American college bar district showed that bar patrons who had consumed AmED had a three-fold increased risk of leaving an establishment highly intoxicated (BrAC ≥ 0.080%) and a four-fold increased risk of intending to drive while intoxicated compared to other bar patrons (Thombs et al., 2010). Similarly, O'Brien et al. (2008) found that AmED users were generally more likely to report: (i) being taken advantage of sexually, (ii) taking advantage of someone sexually, (iii) driving while intoxicated, (iv) riding with a driver under the influence of alcohol, and (v) being hurt, injured, or required medical treatment.

Overall, these studies suggest greater risk-taking by AmED consumers. However, risk-taking behaviour cannot be attributed to the pharmacological effects of AmED as, with the exception of Thombs et al.'s (2010) study, the outcomes reflect risk-taking across all alcohol drinking sessions. In the case of Thombs et al.'s (2010) study, the number of consumers who undertook the risk behaviour is not known. Furthermore, few studies have controlled for systematic individual differences (e.g., risk-taking propensity, sensation-seeking) between consumer types which could account for differences in risk-taking behaviour.

Within-subject comparisons of risk-taking in AmED versus alcohol drinking sessions circumvent these issues by controlling for individual differences between consumer types. However, the two studies published to date have shown mixed results. A study of American university athletes revealed that AmED users scored significantly higher on the Brief Comprehensive Effects of Alcohol questionnaire when reporting risk-taking expectations for AmED compared to alcohol drinking sessions (Woolsey et al., 2010). However, retrospective report of actual risk-taking

behaviour in AmED and alcohol sessions was not undertaken. In contrast, a recent Australian community survey showed that AmED users reported significantly lower odds of engaging in 26 risk behaviours when consuming AmED relative to alcohol in the preceding six months (Peacock et al., 2012). To date, there has been no objective measurement of risk-taking following AmED ingestion. While laboratory-based risk-taking assessment may reduce ecological validity, the controlled environment permits direct measurement of the pharmacological effects of AmED.

Given the divergent findings regarding AmED-induced intoxication misperception and lack of objective assessment of risk-taking outcomes following AmED consumption, the aims of the present study were to assess the effect of a moderate alcohol and ED dose on: (i) subjective measures of intoxication, and (ii) objective measures of risk-taking.

6.4 Materials and Methods

6.4.1 Participants

Twenty-eight healthy right-handed adults (14 males) aged between 18 and 25 years (*M*=19.5, *SD*=1.8) participated in one 90-minute familiarisation session and four 180-minute experimental sessions. The sample comprised self-reported regular caffeine (consumption of 5-28 caffeinated products per week) and ED (minimum consumption of one ED in the preceding month; maximum consumption of one ED per day in the preceding month) consumers. Exclusion criteria pertained to consumption of less than two standard alcoholic drinks in the preceding fortnight or an Alcohol Use Disorders Identification Test (AUDIT; Babor et al., 2001) score of 16 or higher. All participants recorded a body mass index between 18 and 30 and

reported English as a first language, normal sleep patterns, normal or corrected-to-normal vision, and no history of substance abuse, neurological condition, or other serious physical condition. Exclusion was based on: (i) psychiatric diagnosis or Kessler Psychological Distress Scale (K10; Kessler et al., 2002) score of 30 or higher, and (ii) significant intellectual disability or Wechsler Test of Adult Reading (WTAR; Wechsler, 2001) quotient lower than 70. Additional self-report exclusion criteria concerned current regular tobacco or prescription medication use (excluding the contraceptive pill), or illicit drug use in the preceding fortnight. No female participants self-reported being pregnant or currently lactating.

Recruitment occurred via university noticeboard advertisements; volunteers provided informed consent before participation. Ethics approval was granted by the Social Science Human Research Ethics Committee (Tasmania) Network. Participants received an honorarium of 30 AUD and task reimbursement (maximum 20 AUD) per experimental session.

6.4.2 Apparatus and Materials

6.4.2.1 Alcohol, Caffeine, and Energy Drink Intake Measures

The Timeline Follow-Back (Sobell & Sobell, 1992) assessed alcohol consumption patterns. Participants provided retrospective daily standard alcoholic drink intake estimates for the preceding 30 days. Outcomes included: (i) total days consumed alcohol, (ii) total days alcohol consumption exceeded National Health and Medical Research Council's (2009) lifetime low-risk guideline (i.e., three or more standard drinks per session), (iii) total days alcohol consumption exceeded National Health and Medical Research Council's (2009) session low-risk guidelines (i.e., five or

more standard drinks per session), (iii) average standard drinks per drinking day, and (iv) maximum standard drinks per drinking day.

A Caffeine and Energy Drink Use Questionnaire (CEDUQ) assessed average daily caffeine intake (mgs); caffeine content of foods and beverages was based on the Food Standards Australia New Zealand (2010) nutrient database or product packaging. ED consumption patterns in the preceding 30 days were determined by self-report of: (i) ED use frequency, (ii) typical ED intake per drinking day, and (iii) maximum ED intake per drinking day. ED estimates were expressed in standard sizes, where one standard drink was equivalent to 250mL ED containing 80mg caffeine.

6.4.2.2 Risk-Taking Measures

The Balloon Analogue Risk Task (BART; Lejuez et al., 2002) is an objective measure of sequential risk-taking operated via Inquisit Version 3.0.6.0 software. Significant moderate positive correlations have been observed between the BART and self-reported real-world risk behaviours, including alcohol and substance use, cigarette use, gambling, aggressive and antisocial behaviour, sexual and driving risk-taking (Aklin, Lejuez, Zvolensky, Kahler, & Gwadz, 2005; Lejuez et al., 2003a; Lejuez, Aklin, Zvolensky, & Pedulla, 2003b; Lejuez et al., 2002). In the present study, participants clicked on a pump to inflate a simulated balloon 1^{o} and accrue 5 cents in a temporary bank. If the balloon was inflated beyond its pre-determined break point all accrued money was lost; if pumping was discontinued prior to the break point, the accrued money was added to a permanent bank. Participants completed 30 balloons, each with a different explosion probability based on a

variable ratio schedule (average breakpoint 64 pumps; see Lejuez et al. (2002) for details of the algorithm). Thus, each pump increased the accrued amount of money to be lost while decreasing the relative gain of additional pumps. Random selection of a trial number (1-30) at task cessation determined task reimbursement. The primary dependent risk-taking measure was the adjusted average number of balloon pumps (i.e., average number of pumps excluding those trials in which the participant was forced to stop pumping due to balloon explosion). Number of explosions and total earnings were also recorded.

The Risk-Taking Questionnaire-18 items (RT-18; de Haan et al., 2001) required participants to indicate the accuracy of nine statements assessing risk behaviour and nine statements measuring risk assessment using a forced choice dichotomous response format (yes, no). Item score summation resulted in Risk Behaviour and Risk Assessment subscale scores (score range 0-9), with higher subscale scores indicative of greater behavioural risk-taking and less consideration of the consequences of risk-taking, respectively.

6.4.2.3 Subjective Intoxication Measures

The Biphasic Alcohol Effects Scale (BAES; Martin et al., 1993) assessed the subjective biphasic stimulation and sedation effects of alcohol. Participants rated the degree to which they were currently experiencing seven stimulant (e.g., ‘energized’) and seven sedation (e.g., ‘sluggish’) adjectives on an 11-point Likert scale (0 ‘not at all’ to 10 ‘extremely’), with higher subscale scores (score range 0 to 70) indicating greater intensity of stimulation and sedation.

A Subjective Effects Scale (SES) assessed participants' perception of the effects of each treatment. Participants rated their level of intoxication, impairment, mental fatigue, and ability to drive on four 100-mm visual analogue scales with left (0mm) and right (100mm) anchors designated 'not at all' and 'very much' (Beirness, 1987; Marczinski et al., 2011).

The Beverage Rating Scale (BRS; Fillmore & Vogel-Sprott, 2000) assessed participants' perceived alcohol and ED intake. Participants indicated the number of bottles of beer containing 4.8% alcohol (scale range 0 to 10) and number of standard 250mL EDs containing 80mg caffeine (scale range 0 to 3) consumed during beverage administration.

6.4.3 Treatment Conditions

Participants were randomly assigned a counterbalanced treatment administration order. While ED administration was double-blind, alcohol administration was single-blind. Doses were determined by body weight. The active alcohol conditions comprised 0.50g/kg vodka (37.5% alcohol/volume Smirnoff Red Label®, No. 21; Smirnoff Co.), reduced to 85% for female participants (Pihl, Paylan, Gentes-Hawn, & Hoaken, 2003), with an intended peak BrAC of .050%, the Australian legal limit for drink-driving. The active ED dose was 3.57ml/kg Red Bull® (Red Bull GmbH), equivalent to one standard 250ml ED per 70kg person. The placebo alcohol condition was 5ml vodka floated on each portion, with a light alcohol mist sprayed on the inner container (Marczinski & Fillmore, 2006). The placebo ED dose was 3.57mL/kg Red Bull® minus caffeine, taurine, glucuronolactone, inositol, and B vitamin complex; active and placebo ED beverages were matched for sugar content

(i.e., 27g/250mL). Vodka and Red Bull® were administered as a recent Australian survey study demonstrated that these are the most commonly used AmED constituents (Peacock et al., 2013a).

6.4.4 Procedure

6.4.4.1 Familiarisation Session

Following initial eligibility confirmation, participants attended the familiarisation session where they provided informed consent, completed additional screening assessments and sample characteristic measures, and practiced the BART.

6.4.4.2 Experimental Sessions

Experimental sessions were conducted between 0930 and 1900 and separated by a minimum of two and maximum of 10 days. With the exception of consuming a standard breakfast bar 90 minutes prior to session commencement, participants fasted for four hours and abstained from caffeine for eight hours, alcohol and prescription medication for 24 hours, and illicit drugs for the duration of participation. Participants signed a declaration confirming compliance and a zero breath alcohol concentration (BrAC) was verified using an Alcolizer HH-2 (Alcolizer Pty Ltd) prior to session commencement.

After completing baseline BAES and SES measures, participants were administered the beverage in two portions served in opaque lidded cups, consuming each portion at an even pace within a five-minute period. The BAES and SES were re-administered 30 minutes after commencing beverage consumption and the BART

was commenced at 40 minutes; BrAC was recorded at these time points and at the conclusion of the BART (55 minutes). As three additional behavioural tasks were administered, subjective intoxication and BrAC were reassessed 125 minutes after beverage administration.

At each session's completion, participants received a detoxification meal and remained at leisure until recording two consecutive BrAC measurements of 0.03% or less over 15 minutes; debriefing occurred on conclusion of participation.

6.4.5 Data Analysis

Data were analysed blind in IBM SPSS Statistics 19. Due to technical malfunction during electronic survey administration, two participants had missing data for the BAES and SES (N=26) and one participant had missing data for the BRS (N=27). Sample characteristics, objective risk-taking outcomes (BART adjusted average number of pumps, number of explosions, total earnings), and BRS ratings were analysed using 2 (Alcohol: Active, Placebo) x 2 (ED: Active, Placebo) repeated measures ANOVAs. Identical analyses were conducted for BAES and SES outcomes, with the dependent variables in these cases being change from baseline scores calculated for each time point (30 and 125 minutes post-beverage administration). An additional variable, Sex, was included in all analyses. Alpha levels were maintained at p<.050, with Bonferroni adjustments for follow-up paired and independent sample t-tests where necessary. Effect size was calculated using Hedges' g (Hedges, 1981). Pearson product moment coefficients were calculated to determine the relationship between trait and objective risk-taking measures.

6.5 Results

6.5.1 Demographic Characteristics and Self-Reported Alcohol, Caffeine, and Energy Drink Use

The demographic characteristics and self-reported alcohol, caffeine, and ED intake outcomes are displayed in Table 1. While the mean AUDIT score matched the cut-off score indicative of hazardous and harmful alcohol use (Babor et al., 2001), participants generally displayed above-average intelligence, low psychological distress, and a normal body mass index (World Health Organisation, 2006). Participants consumed alcohol on a twice-weekly basis in the preceding month, typically ingesting five standard alcoholic drinks (ten standard drinks during maximum intake sessions), and exceeding the National Health and Medical Research Council (2009) lifetime and session low-risk guidelines on a weekly and fortnightly basis respectively. The sample generally comprised moderate caffeine consumers. One-quarter (29%) ingested EDs on a monthly or less basis and one-third (32%) on a fortnightly to weekly basis; more frequent use was reported by two-fifths (39%) of the sample. Typical ED intake fell within the Australian New Zealand Food Authority (2009) recommendations; these daily intake guidelines were exceeded in maximum ED drinking sessions.

Table 1

Demographic Characteristics and Self-Reported Alcohol Use, Caffeine and ED Use (Standard Deviation in Parentheses; N=28)

Outcome[a]	**Mean (*SD*)**	**Range**
Harmful alcohol use (AUDIT score)	8.1 (3.0)	3.0-14.0
Psychological distress (K10 score)	15.8 (3.3)	12.0-26.0
Intellectual functioning (WTAR IQ)	106.4 (10.3)	87.0-126.0
Body mass index	23.6 (3.0)	18.3-30.0
TLFB Alcohol Use (past month):		
Days any alcohol	7.5 (5.2)	2.0-23.0
Days exceed NHMRC lifetime low-risk guideline	4.4 (2.6)	0.0-10.0
Days exceed NHMRC session low-risk guideline	2.7 (2.3)	0.0-9.0
Average standard alcoholic drinks per drinking day	5.2 (3.2)	1.3-14.9
Maximum standard alcoholic drinks per drinking day	9.6 (5.1)	1.9-22.0
Caffeine/Energy Drink Use:		
Average daily caffeine intake (mg)	236.1 (130.8)	70.4-556.7
Average standard EDs (last month)	1.3 (0.6)	1.0-3.0
Maximum standard ED (last month)	2.4 (1.3)	1.0-6.0

Note. [a]Alcohol Use Disorders Identification Test (AUDIT) score range is 0-40, with a score of 16 or more indicative of hazardous or harmful alcohol use; Kessler Psychological Distress Scale (K10) score range is 10-50, with scores of 30 or higher indicative of a moderate to severe psychological distress; Wechsler Test of Adult Reading (WTAR) standardised score is 100, with higher scores indicative of higher levels of general pre-morbid intellectual functioning; body mass index indicates a greater body mass, with scores between 17 and 29.9 indicating mild-thinness to pre-obese body mass; the Timeline Follow Back (TLFB) reflects participants' alcohol consumption in the preceding month; National Health and Medical Research Council (NHMRC) lifetime low risk guideline is a maximum of two standard alcoholic drinks on any day; NHMRC session low risk guideline is a maximum of four standard alcoholic drinks on any day; the Caffeine Energy Drink Use Questionnaire (CEDUQ) definition of a standard energy drink (ED) was 250ml ED containing approximately 80mg caffeine.

Table 2

Breath Alcohol Concentration, BART Adjusted Average Number of Pumps, Total Earnings, and Number of Explosions, and Beverage Rating Scale Outcomes According to Treatment Condition (Breath Alcohol Concentration and BART N=28; Beverage Rating Scale N=27)

Outcome	Placebo		ED		Alcohol		AmED	
	M	***SD***	***M***	***SD***	***M***	***SD***	***M***	***SD***
Breath Alcohol Concentration:								
30 minutes (Subjective Intoxication Measures)	-	-	-	-	.068	.019	.067	.018
40 minutes (BART Commencement)	-	-	-	-	.062	.014	.064	.014
55 minutes (BART Conclusion)	-	-	-	-	.058	.011	.060	.007
125 minutes (Subjective Intoxication Measures)	-	-	-	-	.039	.009	.040	.007
Balloon Analogue Risk Task:								
Total Earnings	35.3	7.7	38.7	9.3	38.4	9.2	37.3	7.5
Number of Explosions	10.3	4.0	10.4	4.8	9.4	3.8	10.6	4.7
Beverage Rating Scale:								
Number of Standard Alcoholic Drinks	0.3	0.4	0.6	0.8	2.8	1.0	2.9	1.2
Number of Standard Energy Drinks	1.2	0.7	1.0	0.6	1.2	1.1	1.0	0.8

Note. No detectable breath alcohol concentrations were recorded in placebo and ED conditions. The Beverage Rating Scale range for alcoholic drinks and standard EDs was 0-10 and 0-3 respectively; an alcoholic drink unit was 4.8% a/v and a standard ED was 250ml ED containing approximately 80mg caffeine. BART: Balloon Analogue Risk Task; ED: energy drink; AmED: alcohol mixed with energy drink.

6.5.2 Breath Alcohol Concentration

As no detectable BrACs were recorded in placebo alcohol conditions, analyses comprised a 2 (Condition: Alcohol, AmED) x 4 (Time: 30, 40, 55, 125 minutes) repeated measures ANOVA. The main effect of Time was significant, $F(3,81)=62.674$, $p<.001$, with BrAC descending throughout the session (Table 2). No significant main effect of Condition or Condition x Time interaction was observed (*p*s>.631). There was no significant difference in BrAC by Sex (*p*s>.258).

6.5.3 Risk-Taking Outcomes

6.5.3.1 Balloon Analogue Risk-Task

The adjusted average number of pumps for each treatment condition is displayed in Figure 1. While there was no significant main effect of Alcohol ($p=.921$, $g=0.01$), there was a significant main effect of ED, $F(1,27)=4.335$, $p=.047$, $g=0.28$, revealing a small magnitude increase in the adjusted average number of pumps in active ($M=44.5$, $SD=40.3$) relative to placebo ($M=40.3$, $SD=12.8$) ED conditions. There were no interactive effects of alcohol and ED, as evidenced by a non-significant Alcohol x ED interaction ($p=.387$).

Similarly, the main effect of Alcohol and the Alcohol x ED interaction were not significant for total earnings and number of explosions (*p*s>.117) (Table 2), nor was there any significant main effect of ED for these variables (*p*s>.364, *g*s>0.17). There was no significant difference in the adjusted average number of pumps, total earnings, or number of explosions according to Sex (*p*s>.163).

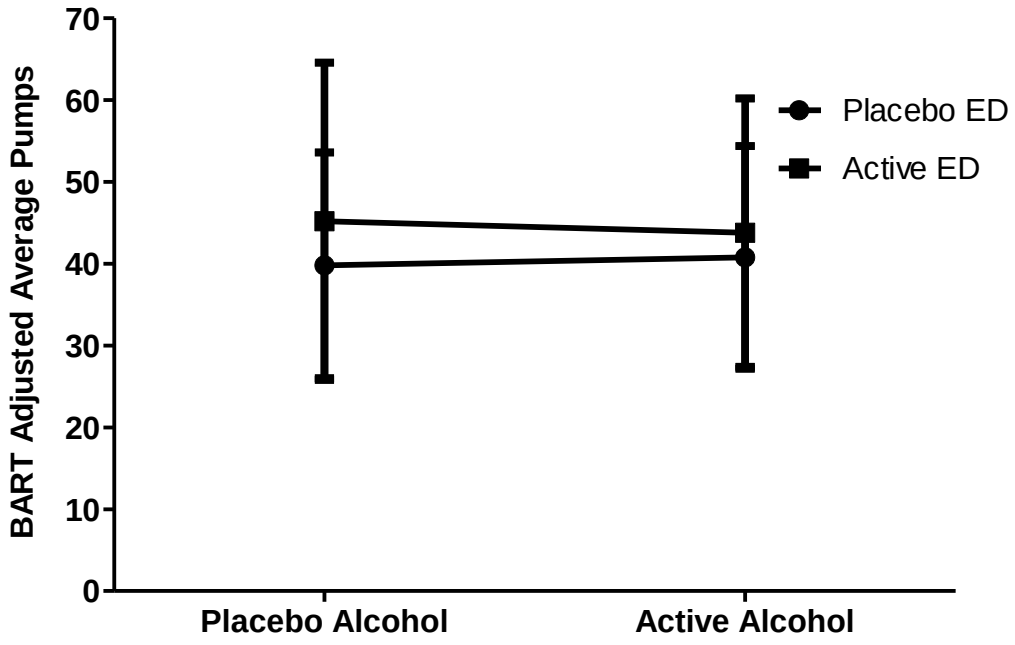

Figure 1. Mean Balloon Analogue Risk Task (BART) adjusted average number of pumps for each treatment condition (*N*=28). Errors bars depict the standard deviation.

6.5.3.2 RT-18

Table 3 displays participants' mean RT-18 subscale scores and the correlation between the RT-18 and BART adjusted average number of pumps. The correlations indicate negligible to weak associations between the RT-18 subscale scores and BART adjusted average number of pumps, with no consistent pattern across treatment conditions.

Table 3

Mean RT-18 Risk Behaviour and Risk Assessment Subscale Scores, and Correlations with Adjusted Average Number of Pumps According to Treatment Condition (Standard Deviation in Parentheses; N=28)

RT-18 Subscale	M (*SD*)	Adjusted Average Number of BART Pumps			
		Placebo	***ED***	***Alcohol***	***AmED***
Risk Behaviour	4.4 (2.2)	.088	.139	.053	-.197
Risk Assessment	3.3 (2.7)	-.201	.214	-.068	.211

Note. RT-18 subscale score range is 0-9, with higher scores indicative of greater risk behaviour and risk assessment respectively on a continuum basis. ED: energy drink; AmED: alcohol mixed with Energy Drink.

6.5.4 Subjective Intoxication Measures

6.5.4.1 Biphasic Alcohol Effects Scale

Table 4 shows the mean BAES stimulation and sedation subscale change scores according to treatment condition. There was a significant main effect of Alcohol on stimulation ratings 30 minutes post-beverage consumption, $F(1,25)=6.303$, $p=.019$, $g=0.47$, with a moderate magnitude increase in stimulation ratings in active ($M=7.4$, $SD=12.5$) relative to placebo ($M=2.1$, $SD=9.5$) alcohol conditions; no significant main effect of Alcohol was evident at 125 minutes ($p=.392$, $g=0.17$). However, a significant Alcohol x ED interaction at 30 minutes was also observed, $F(1, 25)=8.447$, $p=.008$; follow-up comparisons revealed that stimulation ratings were significantly higher in the AmED condition relative to the alcohol condition ($p=.007$, $g=.51$), as well as the ED ($p<.001$, $g=0.84$) and placebo ($p=.008$, $g=0.68$) conditions. There was no significant Alcohol x ED interaction at 125 minutes ($p=.850$). The main effect of ED was not significant for stimulation ratings at 30 ($p=.075$, $g=0.30$) or 125 ($p=.105$, $g=0.26$) minutes.

While there was a trend towards a significant main effect of Alcohol on sedation ratings 30 minutes post-beverage ingestion (p=.057, g=0.52), with higher ratings in the active relative to placebo alcohol conditions, a significant main effect of Alcohol was observed at 125 minutes, $F(1,25)=4.877$, p=.037, g=0.57, with moderate magnitude increase in sedation ratings in active (M=5.9, SD=8.7) relative to placebo (M=0.9, SD=8.7) alcohol conditions. The Alcohol x ED interaction was not significant at either time points (ps>.587), nor was the ED main effect (ps>.137, gs<0.28). There was no significant differences according to Sex for BAES stimulation (ps>.092) or sedation ratings (ps>.093).

6.5.4.2 Subjective Effects Scale

The SES ratings according to treatment condition are displayed in Table 4.

6.5.4.2.1 Intoxication Ratings

There was a significant main effect of Alcohol on intoxication ratings at 30 minutes, $F(1,25)=85.950$, p<.001, g=2.20, and 125 minutes, $F(1,25)=20.932$, p<.001, g=1.10, following beverage administration, with large magnitude increases in intoxication ratings recorded in active (M=46.8, SD=27.9 and M=20.9, SD=27.7) relative to placebo (M=1.1, SD=11.1 and M=-2.2, SD=8.5) alcohol conditions. However, the Alcohol x ED interaction was not significant at either time point (ps>.156), nor was the main effect of ED (ps>.689, gs<0.07). While analyses according to Sex revealed a significant Alcohol x Sex interaction at the later time point, $F(1,24)=4.280$, p=.049, no follow-up tests were significant (ps>.148); there were no other significant differences according to Sex (ps>.169).

Table 4

Treatment Condition Baseline Ratings and Change from Baseline Ratings at 30 Minutes and 125 Minutes Post-Beverage Administration for BAES Stimulation and Sedation Subscales and Subjective Effects Scale Item (Standard Deviation in Parentheses, N=26)

Outcome	Baseline				30 minutes				125 minutes			
	Placebo	***ED***	***Alcohol***	***AmED***	***Placebo***	***ED***	***Alcohol***	***AmED***	***Placebo***	***ED***	***Alcohol***	***AmED***
BAES Stimulation	11.8 (11.6)	9.5 (11.2)	10.4 (10.0)	10.0 (8.8)	2.5 (12.3)	1.8 (8.8)	3.9 (15.1)	10.9 (12.6)	-1.0 (15.1)	1.4 (10.7)	-3.3 (14.1)	0.0 (12.9)
BAES Sedation	19.9 (12.6)	23.4 (14.9)	20.9 (12.7)	21.0 (10.8)	-2.3 (9.1)	-0.6 (0.2)	1.8 (11.8)	4.3 (10.5)	2.5 (12.0)	-0.7 (8.6)	6.5 (12.5)	5.2 (10.9)
SES Intoxication	1.3 (6.3)	4.9 (15.5)	4.1 (13.8)	2.8 (9.9)	1.4 (6.9)	0.9 (19.9)	45.3 (31.5)	48.4 (30.0)	-0.4 (6.9)	-3.9 (16.0)	18.5 (29.5)	23.2 (29.9)
SES Impairment	4.2 (12.4)	4.4 (14.4)	5.5 (14.4)	6.4 (16.7)	-0.4 (10.0)	1.7 (18.3)	33.9 (32.5)	37.5 (32.4)	2.9 (11.4)	0.7 (18.3)	20.0 (27.2)	18.9 (26.1)
SES Mental Fatigue	13.2 (20.9)	9.9 (14.0)	12.5 (19.6)	12.3 (20.0)	0.9 (15.1)	0.3 (16.4)	6.8 (20.3)	6.6 (12.5)	12.8 (23.9)	8.6 (22.1)	18.0 (25.5)	16.6 (22.6)
SES Ability to Drive	86.9 (24.7)	70.9 (41.1)	79.7 (34.4)	75.2 (36.8)	-13.2 (19.4)	-6.2 (35.4)	-55.8 (37.3)	-50.3 (36.4)	-14.0 (22.2)	-5.0 (37.0)	-43.6 (32.9)	-43.6 (33.1)

Note. BAES subscale scores ranged from 0-70, with higher scores indicating greater stimulation/sedation. SES item scores ranged from 0-100 with higher scores indicating greater intensity of intoxication, impairment, and mental fatigue/reduced ability to drive. Note that BAES and SES scores represent the change from baseline. ED: energy drink; AmED: alcohol mixed with energy drink; BAES: Biphasic Alcohol Effects Scale; SES: Subjective Effects Scale.

6.5.4.2.2 Impairment Ratings

Similarly, there was a significant main effect of Alcohol on impairment ratings at 30 minutes, $F(1,25)=47.688$, $p<.001$, $g=1.72$, and 125 minutes, $F(1,25)=18.315$, $p<.001$, $g=0.97$, following beverage administration, with large magnitude increases in impairment ratings in active ($M=35.7$, $SD=27.3$ and $M=19.4$, $SD=22.9$, respectively) relative to placebo ($M=0.6$, $SD=8.8$ and $M=1.8$, $SD=11.7$, respectively) alcohol conditions. The Alcohol x ED interaction was not significant at either time point (ps>.865), nor was the main effect of ED significant (ps>.434, gs<0.16). While analyses according to Sex revealed a trend towards significant Alcohol x Sex interaction at 125 minutes, $F(1,24)=3.679$, $p=.067$, no follow-up tests were significant (ps>.240), nor were any other interactions involving Sex significant (ps>.265).

6.5.4.2.3 Mental Fatigue Ratings

There was no significant main effect of Alcohol on mental fatigue ratings at 30 ($p=.062$, $g=0.53$) or 125 ($p=.125$, $g=0.39$) minutes after beverage consumption. The Alcohol x ED interaction was not significant at either time point (ps>.761), nor was the main effect of ED significant (ps>.544, gs<0.16). There was no significant difference in mental fatigue ratings according to Sex (ps>.273).

6.5.4.2.4 Ability to Drive Ratings

There was a significant main effect of Alcohol on ratings of ability to drive at 30 minutes, $F(1,25)=50.525$, $p<.001$, $g=1.54$, and 125 minutes, $F(1,25)=31.637$, $p<.001$, $g=1.40$, with large magnitude decreases in ability to drive in active ($M=-53.0$, $SD=32.1$ and $M=-43.6$ and $SD=26.0$, respectively) relative to placebo ($M=-9.7$,

SD=23.1 and *M*=-9.5, *SD*=22.5, respectively) alcohol conditions. However, the Alcohol x ED interaction (*p*s>.439) and the main effect of ED (*p*s>.221, *g*s<0.23) were not significant across testing points. There was no significant difference in ratings of ability to drive according to Sex (*p*s>.196).

6.5.3 Beverage Rating Scale

Mean alcohol and ED beverage ratings at 125 minutes are displayed in Table 2. There was a significant main effect of Alcohol for perceived alcohol intake, $F(1,26)=152.164$, $p<.001$, $g=3.13$, with greater alcohol intake reported in active (*M*=2.9, *SD*=1.0) relative to placebo (*M*=0.50, *SD*=0.49) alcohol conditions. However, the Alcohol x ED interaction was not significant (*p*=.532), nor was the main effect of ED (*p*=.054, *g*=0.33). Analyses according to Sex revealed a trend towards a significant Alcohol x Sex interaction, $F(1,25)=3.740$, $p=.065$; follow-up tests showed that perceived active alcohol intake in alcohol conditions tended to be greater for males (*M*=3.2, *SD*=1.0) compared to females (*M*=2.5, *SD*=0.8) (*p*=.065, *g*=0.77); however, there were no sex differences in relation to perceived alcohol intake in placebo alcohol conditions (*p*=.706). There were no other significant effects involving Sex.

There was no significant main effect of Alcohol (*p*=.946, *g*=0.02), Alcohol x ED interaction (*p*=.958), or main effect of ED (*p*=.142, *g*=0.25) on perceived ED intake. There was no significant difference in perceived ED intake according to Sex (*p*s>.457).

6.6 Discussion

The results of the present study revealed an interactive effect of alcohol and EDs on perceived stimulation, with greater stimulation ratings in the AmED relative to the alcohol condition at 30 minutes post-beverage administration. However, no interactive effects of alcohol and ED were observed for perceived sedation, impairment, mental fatigue, ability to drive and, most importantly, intoxication; with the exception of mental fatigue ratings, treatment effects were restricted to the independent effects of alcohol. Despite the escalation in perceived alcohol-induced impairment, a moderate alcohol dose (mean BrAC .062%) did not alter risk-taking behaviour, nor did the interaction of alcohol and ED (mean BrAC .064%). While there was a significant increase in risk-taking evident in active relative to placebo ED conditions, the magnitude of difference was small.

The current results align with previous research involving moderate alcohol doses (peak mean BAC .071% to .089%) regarding the absence of an interactive alcohol and ED effect on perceived sedation, intoxication, impairment, and ability to drive (Marczinski et al., 2011; Marczinski et al., 2012). In regards to perceived stimulation, the authors of these studies reported an interactive effect of alcohol and EDs, with greater stimulation ratings observed in AmED conditions. In the study by Marczinski et al. (2011), the reported interactive AmED effect was based on examination of descriptive data rather than direct statistical comparison of ratings in AmED and alcohol conditions. In contrast, in the study by Marczinski et al. (2012), ratings were only provided post-beverage administration, meaning that baseline differences between treatment conditions in subjective state may have confounded outcomes. While conclusions regarding AmED-induced enhancement of stimulation

have been challenged on the basis of these limitations (Peacock & Bruno, 2013), the present study aligned with the interpretation of Marczinski et al. (2011) and Marczinski et al. (2012) in that a significant moderate magnitude increase in perceived stimulation was evident 30 minutes after consumption of AmED relative to alcohol. These results also support those of Attwood et al. (2012), who observed greater stimulation ratings following co-ingestion of caffeine (2.0mg/kg) with alcohol (0.6g/kg) relative to independent alcohol ingestion, with no significant difference in ratings of intoxication. As such, Attwood et al. (2012) concluded that caffeine may change the nature, as opposed to the degree, of intoxication; this same conclusion could be tentatively applied to the present subjective outcomes.

As the stimulant effects of alcohol are a major predictor of subsequent alcohol intake (Rossheim & Thombs, 2011), ED-enhancement of alcohol-induced stimulation could heighten the reinforcing effects of alcohol and increase alcohol intake. However, previous survey research has yielded mixed support; while Australian and Canadian studies have shown significantly greater alcohol intake in AmED sessions relative to alcohol sessions (Peacock et al., 2012; Price et al., 2010), a United States study revealed the converse (Woolsey et al., 2010). Marczinski et al. (2013) found that ED (1.82mL/kg) co-ingested with alcohol (0.91mL/kg; peak mean BrAC .043%) increased subjective ratings of ‘desire for more alcohol’ across more time-points post-drink than alcohol only, suggesting that EDs may increase alcohol priming. However, between-condition analyses revealed no significant difference in ratings between alcohol and AmED conditions (Marczinski et al., 2013).

As such, conclusions regarding enhanced reinforcement of the pleasurable effects of alcohol by ED co-ingestion remain tentative until laboratory studies are undertaken examining: (i) the dose-dependent effect of 'real-life' doses on subjective intoxication indices, and (ii) the effect of AmED-increased stimulation enhancement on subsequent alcohol intake (Peacock & Bruno, 2013), particularly in light of the moderate alcohol dose administered in the present study . While previous research has generally involved administration of a set dose (approximately one standard 250mL ED per 70kg person), research by Peacock et al. (2012) revealed that AmED consumers were typically ingesting 7.1 standard alcoholic drinks and 2.4 standard 250mL EDs in AmED drinking session. As such, studies seeking to provide policy advice should extend further into these high dosage domains for ecological validity, and because the propensity for risky behaviours is inflated at such high alcohol consumption levels (National Health and Medical Research Council, 2009), as is the potential for more complex interactive effects of ED and alcohol.

In light of the equivalent perception of intoxication and impairment in AmED and alcohol conditions, it is not surprising that objective measurement of risk-taking revealed no interactive effect. These results partly contradict self-reported risk taking behaviour: Woolsey et al. (2010) observed an increased expectation of risk-taking for AmED relative to alcohol drinking sessions, whereas Peacock et al. (2012) found lower odds of risk-taking in AmED relative to alcohol drinking sessions. However, in the present study, alcohol consumption did not alter risk-taking, regardless of the presence or absence of ED. Experimental research assessing the impact of alcohol on risk-taking has yielded equivocal results, with some studies revealing increased risk-taking (Lane et al., 2004); Liguori, D'Agostino, Dworkin, Edwards, and Robinson

(1999) while others have shown no significant effect (Breslin & Sobell, 1999; George et al., 2005). The present results could be attributed to the moderate dose (0.5g/kg) administered. For example, Lane et al. (2004) reported that alcohol (0.2g/kg, 0.4g/kg, and 0.8g/kg) dose-dependently increased selection of the risky response option in a gambling task, with the highest dose increasing the probability of consecutive losing risky responses following a win on a risky response. Thus, the administered alcohol dose may not have been sufficient to result in detection of alcohol-induced impairment.

However, the sensitivity of the BART could also explain the current results. Unlike other behavioural measures, the BART conceptualises risk-taking as occurring on a continuum, with risk-taking becoming disadvantageous only at a certain point which varies according to the circumstances (Lejuez et al., 2003a). Thus, the BART is advised for administration in nonclinical populations, as it captures risky behaviour that is not necessarily disadvantageous (Skeel, Pilarski, Pytlak, & Neudecker, 2008). However, despite significant correlations with self-reported real-world substance use behaviours (Aklin et al., 2005; Lejuez et al., 2003a; Lejuez et al., 2003b), the BART has not consistently detected the acute effects of drugs on risk-taking. For example, Reynolds et al. (2006b) found that acute alcohol doses of 0.4g/kg and 0.8g/kg did not impact performance on the BART. As such, replication of the present study with an alternate measure of behavioural risk-taking may clarify the effect of acute AmED consumption on risk-taking.

The detection of a small magnitude increase in risk-taking following ED administration indicates that AmED can increase risk-taking via the ED component.

However, the small magnitude of the effect calls into question the practical implications for ED and AmED consumers. It is not known whether the effects of EDs on risk-taking would increase in magnitude with an increasing ED dose, or, indeed, with an increasing alcohol dose. Thus, further clarification is required assessing the dose-dependent effects of AmED on objectively measured risk-taking behaviour, to determine: (i) whether the ED effect increases in magnitude with higher doses, and (ii) whether an interactive effect becomes apparent with higher alcohol doses.

The present results also showed negligible correlations between the BART adjusted number of pumps and the RT-18 subscale scores. These results align with several studies revealing no significant correlation between BART outcomes and trait sensation seeking and impulsivity measures (Aklin et al., 2005; Hunt, Hopko, Bare, Lejuez, & Robinson, 2005; Lejuez et al., 2003a; Skeel et al., 2008). The majority of the literature points towards weak associations between psychometric and behavioural impulsivity measures among non-clinical samples, suggesting that the behavioural tendencies identified in self-report and laboratory measures may differ (Lane et al., 2003; Reynolds, Ortengren, Richards, & de Wit, 2006a; Reynolds et al., 2008).

While the present study was single-blind for alcohol administration, several procedures were enforced to minimise experimenter bias, including: (i) implementing systematic structures for participant interaction (e.g., standardised instructions), (ii) double-blinding of ED administration via coding, (ii) use of objective measurement procedures, and (iii) blinding treatment conditions

throughout data processing and analysis. As the perceived alcohol intake in active alcohol conditions was approximately 2.5 standard drinks higher than placebo alcohol conditions, we cannot discount alcohol expectancy effects. However, the perceived alcohol intake and reported ratings of intoxication did not differ significantly for the alcohol and AmED conditions.

Another potential source of bias was the use of the BART adjusted average number of pumps. Although this measure is the primary outcome, trials on which the balloon exploded were excluded, thus discounting the participant's behaviour on that trial and lowering the adjusted average (Euser et al., 2011; Pleskac, Wallsten, Wang, & Lejuez, 2008). While approximately one-third of the trials were excluded across the treatment conditions, there was no significant difference across the treatment conditions in the number of explosions. More reliable estimates could be achieved by use of an automatic response mode, in which participants predetermine the number of pumps, allowing the balloon to automatically inflate until the pumps are completed or the break point is reached (Pleskac et al., 2008).

In conclusion, the present study's results suggest that the interactive effect of a moderate alcohol and low ED dose were restricted to perceived stimulation, with no significant impact on perceived intoxication and impairment relative to alcohol alone. While no interactive AmED effect was evident for objectively measured risk-taking behaviour, there was no effect of alcohol consumption in general on risk-taking outcomes. Engagement in risk-taking behaviour was only increased by ED consumption however the magnitude of the effect suggests negligible implications for ED and AmED consumers. Conclusions regarding the link between AmED and

risk-taking remain tentative until further research is undertaken: (i) using higher doses, and (ii) with alternative validated behavioural measures of risk-taking.

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Chapter 7: Laboratory Behavioural Assessment of Impulsive Behaviour Following an Acute Alcohol and Energy Drink Dose

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7.1 Preface

This chapter outlines the results from an experimental study (*Study 2*) regarding the effect of an acute alcohol and ED dose on three aspects of behavioural impulsivity: impulsive response initiation, response disinhibition, and impulsive decision-making. To date, this is the first study to provide a comprehensive assessment of these aspects of behavioural impulsivity after consumption of alcohol with and without ED. This manuscript extended from *Chapter 6*, in that the aim was to develop an overarching profile of the behavioural outcomes of co-ingestion, extending beyond risk-taking to determine whether there were any state-dependent changes in behavioural impulsivity post-administration (*Question 5.2*). Previous research had indicated that AmED consumers are higher in trait impulsivity than alcohol consumers (Brache & Stockwell, 2011); assessment of state-dependent impulsivity in controlled research settings in this study clarified whether changes in these behaviours may reflect the pharmacological effects of co-ingestion. The results of this study contribute to the development of an evidence-base to determine the potential harms of AmED use and develop appropriate policy responses.

7.2 Abstract

Background: Consumption of alcohol may impair decision-making by increasing behavioural impulsivity. Concerns have been raised about a new consumption trend, alcohol mixed with energy drinks (AmED), specifically regarding the impact of consumption on risk-taking behaviour. Despite this, there has been no comprehensive assessment of AmED-induced changes in behavioural impulsivity. The aim of this study was to determine the effect of an acute alcohol and energy drink (ED) dose on behavioural impulsivity: specifically, impulsive response initiation, response disinhibition, and impulsive decision-making.

Method: Using a placebo-controlled, single-blind, crossover design, participants (*N*=28) attended four sessions where they were administered in counterbalanced order: 0.5g/kg alcohol, 3.57ml/kg ED, AmED, and a placebo beverage. Participants completed the Immediate Memory/Delayed Memory Task (IMT/DMT), a Cued Go/No-Go task, and the Experiential Discounting Task (EDT).

Results: Alcohol-induced increases in impulsive response initiation were reduced by co-ingestion of ED for female participants on the DMT only. This effect was not evident for male participants, or when task difficulty was lower, as assessed by the performance on the IMT. There was generally no effect of alcohol or ED, consumed independently or co-ingested, on the measure of response disinhibition, the Cued Go/No-Go task, or the measure of impulsive decision-making, the EDT.

Conclusions: This study demonstrated that interactive effects of a moderate alcohol and ED dose were dependent on the behavioural impulsivity measure. AmED-induced decreases in elevated impulsive behaviour during intoxication were restricted to impulsive response initiation, evident only for female participants. However, the study may have had reduced sensitivity to interactive alcohol and ED

effects, as the alcohol dose administered may not have been sufficient for detection of changes in response disinhibition and impulsive decision-making.

7.3 Introduction

Impulsivity has been associated with alcohol use initiation, as well as the development and maintenance of alcohol-related disorders (Lejuez et al., 2010). Previous research has yielded differential effects of alcohol on laboratory-based impulsivity measures, suggesting that there are several measurably different processes associated with impulsive behaviour, the number and definition of which remain subject to debate (de Wit, 2009; Dougherty et al., 2005; Evenden, 1999; Meda et al., 2009). Three subtypes identified using laboratory behavioural assessment paradigms include: impulsive response initiation, response disinhibition, and impulsive decision-making (Dougherty et al., 2008; Reynolds et al., 2008).

7.3.1 Impulsive Response Initiation

Impulsive response initiation refers to premature responding to a stimulus prior to completion of stimulus processing, evident via quick responses to non-targets (Dougherty et al., 1999). Impulsive response initiation has commonly been measured using a Continuous Performance Task (CPT) paradigm (Beck et al., 1956). However, researchers have raised concern regarding ceiling effects due to insufficient task difficulty (Cornblatt & Keilp, 1994). The Immediate Memory/Delayed Memory Tasks (IMT/DMT; Dougherty et al., 2002) increase task difficulty by incorporating two non-targets (similar and unrelated to the target). Alcohol generally has a dose-dependent effect on the IMT, with increased impulsive responding detected after high (BrAC .063% to .092%), but not low, doses (BrAC .011% to .056%) (Dougherty et al., 2000b; Dougherty et al., 1999; S. C. Reed et al., 2012). DMT results are more equivocal. Dougherty et al. (1999) and S. C. Reed et al. (2012) reported increased impulsive response initiation following low to high alcohol

dosing (BrAC .035% to .092%). In contrast, Dougherty et al. (2000b) found no effect of a low (BrAC .039%) or high (BrAC .091%) alcohol dose on DMT performance.

7.3.2 Response Disinhibition

Response disinhibition refers to a reduced ability to suppress or withdraw a response (de Wit, 2009). Response disinhibition is based on the theory of cognitive control, whereby successful inhibition during response conflict is the result of a competition between activation and inhibition processes (Gray, 1976; Logan & Cowan, 1984). If the inhibiting process is completed first, the response is suppressed; if the activating process is completed first, the response is executed. Impairment of the former process is thought to be the primary cause of alcohol-induced deficits in behavioural control. Alcohol-induced increases in response disinhibition are indexed by the Cued Go/No-Go task; deficient inhibition is inferred from the proportion of no-go targets which generate a response (Ridderinkhof et al., 2004). Moderate to high alcohol doses (mean peak BrAC .050% to .102%) typically result in appreciable increases in response disinhibition on the Cued Go/No-Go task, evident via a significant increase in the proportion of commission errors to invalid cued 'no-go' targets after alcohol relative to placebo (Marczinski & Fillmore, 2003b; Weafer & Fillmore, 2012a).

7.3.3 Impulsive Decision-Making

Impulsive decision-making refers to a relative preference for immediate outcomes despite the long-term consequences (Reynolds et al., 2008). Impulsive decision-making is measured using a delay-discounting paradigm, where participants choose between small immediate rewards and larger delayed rewards (Logue, 1988;

Rachlin, 1990; Rachlin et al., 1991). Research examining the effect of alcohol on hypothetical delay discounting has revealed mixed findings: Richards et al. (1999b) and Reynolds et al. (2006b) did not detect a significant change in delay-discounting following low to moderate doses (BrAC ~.037% to ~.076%) ; Ortner et al. (2003) found that a moderate dose (BrAC .074%) tended to decrease discounting; and S. C. Reed et al. (2012) found that a moderate to high (BrAC .056% to .092%) alcohol dose increased discounting. However, questionnaire-based assessment has been shown to produce slower rates of discounting relative to operant procedures (Navarick, 2004). The only study to date adopting operant procedures with monetary reinforcement showed greater delay discounting after a moderate (BrAC ~.076%), but not a low (BrAC ~.037%), alcohol dose (Reynolds et al., 2006b).

7.3.4 Alcohol, Energy Drinks, and Aspects of Behavioural Impulsivity

The reviewed research indicates that alcohol selectively impairs behavioural impulsivity. However, there is a dearth of research investigating the interactive effects of alcohol co-ingested with stimulants. An increasingly popular consumption trend, alcohol mixed with energy drinks (AmED), has been theorised to enhance negative alcohol outcomes through: (i) increased quantity and duration of alcohol consumption, and (ii) heightened disinhibition and increased risk-taking (Weldy, 2010). However, the evidence to support these speculations is mixed, particularly in regards to the latter point. Woolsey et al. (2010) found that AmED consumers self-reported greater expectation of risk-taking in AmED relative to alcohol sessions, however no retrospective assessment of actual engagement in risk-taking was undertaken. In contrast, two studies have shown that AmED consumers self-report

significantly lower odds of engaging in risk behaviours in AmED versus alcohol drinking sessions (de Haan et al., 2012; Peacock et al., 2012).

Changes in impulsive behaviour may impact on alcohol-related consequences; an impaired ability to wait for and process information or to evaluate consequences could increase the likelihood of risky behaviours. Despite suggestions that AmED increases risk-taking, there is no evidence to indicate whether ED co-ingestion enhances, reduces, or maintains alcohol-induced impairment of behavioural impulsivity. There has only been one study investigating the effect of AmED on response disinhibition in isolation, with no significant interactive effect of a moderate alcohol (BrAC .081%) and a low ED (3.57mL/kg) dose evident (Marczinski et al., 2011). As such, the aim of the present study was to concurrently compare the effects of an acute alcohol dose administered independently and in combination with ED on impulsive response initiation, response disinhibition, and impulsive decision-making.

7.4 Method

7.4.1 Participants

Participants were 28 (14 male) healthy adults who self-reported regular use of caffeine (consumption of 5-28 caffeinated products per week), ED (minimum consumption of one ED in the preceding month; maximum consumption of one ED per day in the preceding month), and alcohol (minimum consumption of two standard alcoholic drinks in the past fortnight). Participants had normal or correct-to-normal vision and normal sleep patterns, spoke English as a first language, were right-handed, and recorded a body mass index between 18 and 30. Exclusion criteria

pertained to: (i) significant neurological, physical, or psychiatric condition, (ii) current pregnancy or lactation, (iii) regular current tobacco, medication, or illicit drug use, (iv) a score of ≥30 on the Kessler Psychological Distress Scale (Kessler et al., 2002), (ii) a quotient < 85 on the Wechsler Test of Adult Reading, and (iii) a score of ≥16 on the Alcohol Use Disorders Identification Test (Babor et al., 2001). The study was approved by the Human Research Ethics Committee (Tasmania) Network and performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki; informed consent was provided. Participants were reimbursed 30 AUD (plus maximum task reimbursement of 20 AUD) per experimental session.

7.4.2 Measures

7.4.2.1 Impulsive Response Initiation: Immediate and Delayed Memory Tasks

In the IMT (Dougherty et al., 2002) participants pressed a response pad as quickly and accurately as possible when a randomly generated 5-digit sequence matched the preceding sequence (e.g., '38391' followed by '38391'). Stimuli were presented for 500ms with a 500ms inter-stimulus interval (ISI). The stimuli comprised: (i) target, a sequence identical to the preceding sequence (33% probability), (ii) catch, a sequence differing from the preceding sequence by one digit (33% probability), and (iii) filler, a random sequence (34% probability). The DMT followed the same procedure but included a distracter stimulus ('12345') repeated three times between each sequence. The tasks were delivered via Compumedics Neuroscan (2005) software and consisted of one (IMT) and two (DMT) 5-minute testing blocks separated by a 30 second rest; the additional DMT block was run as there was a low number of targets requiring a response due to the inclusion of distracter stimuli.

Impulsive response initiation was indexed as the ratio of commission errors (catch stimuli responses) to correct detections (target responses) (Dougherty et al., 2000b).

7.4.2.2 Response Disinhibition: Cued Go/No-Go Task

The Cued Go/No-Go task was based on the protocol adopted by Randall and Smith (2011) and Marczinski et al. (2011). Each trial consisted of a cue (horizontal or vertical white rectangle) followed by a 'go' or 'no-go' target (green or blue rectangle respectively), each displayed for 200ms. The cue-target stimulus onset asynchrony was fixed at 1000ms; the interval between target and cue varied between 1500 and 2500ms. Participants were instructed to press a response pad when the 'go' target was displayed and suppress the response when the 'no-go' target was displayed. Cue orientation correctly signalled the target on 80% of trials (i.e., a vertical rectangle preceded the green and blue rectangle on 80% (N=160) and 20% (N=40) of trials, respectively). Participants were informed that the cue generally, but not always, indicated the target type. The task comprised four blocks separated by 30 seconds. The primary measure of response disinhibition was the proportion of commission errors to valid and invalid cued 'no-go' targets.

7.4.2.3 Impulsive Decision-Making: Experiential Discounting Task

In the EDT (Reynolds & Schiffbauer, 2004) participants chose between a standard amount (AUD 0.30) that was delayed and probabilistic (35% chance of receiving) versus an immediate and certain adjusting amount. Participants choose between two illuminated light bulbs presented on the screen representing the standard and adjusting choice. Delivery of the reward was indicated by illumination of the bank button. Non-delivery of the standard reward after the elapsed delay was indicated by

re-illumination of the light bulbs to signal a new trial. The adjusting amount started at AUD 0.15; this amount increased for the next choice if the standard choice was selected and decreased if the adjusting amount was chosen (see Reynolds & Schiffbauer, 2004). Participants completed four counterbalanced blocks (0, 7, 14, and 28 second delay). An inter-block interval was implemented once 16 choice trials were completed and an indifference point was established to ensure the block was not ended faster by selecting only the adjusting option; forced-option trials were also included after three consecution selections of either choice to ensure exposure to both choice options. The indifference point was the average adjusting amount for the last six trials where there were equal responses to the standard and adjusting amounts. Task reimbursement was determined by random selection of a block number. Participants' data were coded as missing if an indifference point was not reached. After standardising the indifference point, the total area under the curve (AUC) was calculated as the primary measure of impulsive decision-making (Myerson, Green, & Warusawitharana, 2001).

7.4.2.4 Trait Measures of Impulsivity

Rash impulsivity was assessed via the I_7 Impulsiveness subscale (Eysenck, Pearson, Easting, & Allsopp, 1985), a 19 item scale with a yes/no response format. The Reward Responsiveness and Drive BIS/BAS subscales (Carver & White, 1994) were used to measure impulsive reward drive (Gullo, Ward, Dawe, Powell, & Jackson, 2011). They consisted of 5 and 4 items, respectively, rated on a 4-point Likert scale ('very false for me' to 'very true for me').

7.4.2.5 Beverage Rating Scale

The Beverage Rating Scale (BRS; Fillmore & Vogel-Sprott, 2000) was used as a placebo manipulation check. Participants indicated the number of 4.8% alcoholic drinks (range 0-3, increasing in 0.5 increments) and number of standard 250mL EDs (range 0-3, increasing in 0.5 increments) they believed they had consumed.

7.4.3 Design and Treatment Conditions

A placebo-controlled within-subjects design was employed with single-blind alcohol administration and double-blind ED administration. Participants ingested four counterbalanced treatments: (i) active alcohol and active ED (*AmED*), (ii) active alcohol and placebo ED (*alcohol*), (iii) placebo alcohol and active ED (*ED*), and (iv) placebo alcohol and placebo ED (*placebo*). Active ED comprised 3.57ml/kg Red Bull® (Red Bull GmbH), equivalent to one standard 250ml ED per 70kg person. Placebo ED comprised 3.57mL/kg Red Bull® minus caffeine, taurine, glucuronolactone, inositol, and B vitamin complex. Active and placebo ED were matched for sugar content (i.e., 27g/250mL) and for taste, appearance, and smell. Active alcohol comprised 0.50g/kg vodka (37.5% a/v Smirnoff Red Label®, No. 21; Smirnoff Co.) reduced to 85% for females (Pihl et al., 2003), with an intended peak BrAC of .050%. Placebo alcohol comprised 5ml vodka floated on each portion with an alcohol mist sprayed inside the container (Marczinski & Fillmore, 2006).

7.4.4 Procedure

After completing an online screening questionnaire, participants attended a 90-minute familiarisation session where consent was obtained, sample characteristic measures were completed, and behavioural tasks were practiced. Participants then

attended four 180-minute experimental sessions between the hours of 0930 and 1900 and separated by between 2 and 10 days. Except for consuming a standard breakfast bar 90 minutes prior to each session, participants abstained from food for 4 hours, caffeine for 8 hours, and alcohol for 24 hours prior to each session and illicit drugs for the duration of participation. At each session participants signed a declaration confirming drug abstinence and zero BrAC was verified with an Alcolizer HH-2 breathalyser (Alcolizer Pty Ltd). The beverage was administered in two portions served in opaque lidded cups; each portion was consumed over a five-minute period. BrAC was recorded and the IMT/DMT, Cued Go/No Go task, and EDT and BRS were completed at 55, 75, 100, and 125 minutes following beverage administration, respectively. As part of a companion study, the Balloon Analogue Risk Task (Lejuez et al., 2002) was completed at 40 minutes and electroencephalographic data was collected (Peacock et al., 2013c).

7.4.5 Data Analysis

Statistical analyses were conducted using IBM SPSS Statistics version 21. For the sample characteristics, descriptive statistics were calculated and one-way ANOVAs conducted to ensure similar alcohol group composition. Missing data due to technical malfunction resulted in a smaller dataset for BrAC and the BRS (N=27), and the IMT/DMT and Cued Go/No-Go task (N=26). Nine participants failed to obtain an indifference point for at least one block on the EDT and one participant did not reach an indifference point across all treatment conditions. Behavioural impulsivity outcomes were analysed using Mixed Models for Repeated Measures regression with a diagonal covariance structure to avoid imputing missing data or excluding whole cases. The basic model tested comprised Alcohol (Active, Placebo),

ED (Active, Placebo) and Alcohol x ED as fixed factors. The adjusted model included Subject as a random factor and Sex (Male, Female), Alcohol x Sex, ED x Sex, and Alcohol x ED x Sex as fixed factors. Post hoc pairwise comparisons were conducted for significant two-way interactions; false discovery rate (Benjamini & Hochberg, 1995) was used to control for error rates associated with multiple comparisons. Mixed models were calculated for significant three-way interactions, with breakdown according to Alcohol. A 2 (Condition: AmED, alcohol) x 5 (Time: 30, 55, 75, 100, 125 minutes) x 2 (Sex: Male, Female) mixed ANOVA was conducted for BrAC with Sex as the between-subjects factor; no detectable BrACs were recorded in placebo alcohol conditions. BRS outcomes were analysed using 2 (Alcohol: Active, Placebo) x 2 (ED: Active, Placebo) repeated measures ANOVAs. For all analyses significance levels were maintained at $p<.050$, with $p<.100$ deemed a trend towards significance, and effect sizes were calculated using Hedges' g (Hedges, 1981) where appropriate.

7.5 Results

7.5.1 Sample Characteristics

Participants reported consuming alcohol in excess of National Health and Medical Research Council (2009) session low-risk guidelines of a maximum of four standard alcoholic drinks on a fortnightly basis (Table 1). Their typical ED intake fell within the Food Standards Australia and New Zealand (2009) daily intake guidelines of a maximum of two standard 250mL EDs containing 80mg caffeine. There was some variability in frequency of ED intake: one-quarter (29%) ingested EDs on a monthly or less basis; one-third (32%) on a fortnightly to weekly basis; two-fifths (39%) reported more frequent use.

7.5.2 Breath Alcohol Concentration

Alcohol and AmED peak mean BrAC at 30 minutes were .068% and .067%, respectively. There was no significant main effect of Condition (p=.878) or Sex (p=.836), indicating that BrAC did not differ significantly with co-ingestion of ED. A significant main effect of Time was observed, $F(4,104)=56.75$, $p<.001$, with decrements in BrAC at each subsequent testing point (ps<.010) (Table 2). No interactions reached significance (ps>.275).

7.5.3 Immediate Memory Task

There was a trend towards a significant main effect of Alcohol for the basic model (p=.080); the main effect of ED and Alcohol x ED interaction were not significant (Table 3). The main effect of Alcohol reached significance in the adjusted model (p=.008, g=0.48), with a significant small magnitude increase in IMT ratio in the active (M=.38, SD=.13) versus the placebo (M=.33, SD=.13) alcohol condition. The adjusted model showed no significant main effect of ED and Sex or interaction between Alcohol, ED, and Sex (Figure 1). Simple main effects comparison showed no significant change in IMT ratio according to whether active alcohol was co-ingested with placebo (M=.33, SD=.15) or active ED (M=.38, SD=.15, p=.745, g=0.39).

Table 1

Demographic Characteristics and Self-Reported Alcohol Use, Caffeine and ED Use (Standard Deviation in Parentheses; N=28)

Outcome[a]	**Mean (*SD*)**	**Range**
Age	19.5 (1.8)	18.0-25.0
Harnful alcohol use (AUDIT score)	8.1 (3.0)	3.0-14.0
Psychological distress (K10 score)	15.8 (3.3)	12.0-26.0
Intellectual functioning (WTAR)	106.4 (10.3)	87.0-126.0
Body mass index	23.6 (3.0)	18.3-30.0
TLFB Alcohol Use (past month):		
Days any alcohol	7.5 (5.2)	2.0-23.0
Days exceed NHMRC lifetime low-risk guideline	4.4 (2.6)	0.0-10.0
Days exceed NHMRC session low-risk guideline	2.7 (2.3)	0.0-9.0
Average standard alcoholic drinks per drinking day	5.2 (3.2)	1.3-14.9
Maximum standard alcoholic drinks per drinking day	9.6 (5.1)	1.9-22.0
Caffeine/Energy Drink Use:		
Average daily caffeine intake (mg)	236.1 (130.8)	70.4-556.7
Average standard EDs per ED drinking day (past month)	1.3 (0.6)	1.0-3.0
Maximum standard ED per ED drinking day (past month)	2.4 (1.3)	1.0-6.0
Trait Impulsivity:		
BAS Drive Subscale Score	9.0 (2.2)	5-13
BAS Reward Responsiveness Subscale Score	7.5 (2.2)	5-12
I_7 Impulsivity Subscale Score	6.7 (4.3)	0-16

Note: [a] Alcohol Use Disorders Identification Test (AUDIT; Babor et al., 2001) score range is 0-40, with a score of 16 or more indicative of hazardous or harmful alcohol use; Kessler Psychological Distress Scale (K10; Kessler et al., 2002) score range is 10-50, with scores of 30 or higher indicative of a moderate to severe psychological distress; Wechsler Test of Adult Reading (WTAR) standardised score is 100, with higher scores indicative of higher levels of general pre-morbid intellectual functioning; body mass index indicates a greater body mass, with scores between 17 and 29.9 indicating mild-thinness to pre-obese body mass; the Timeline Follow Back (TLFB; Sobell & Sobell, 1992) reflects participants' alcohol consumption in the preceding month; Natioanl Health and Medical Research Council (NHMRC, 2009) lifetime low risk guideline is a maximum of two standard alcoholic drinks on any day; NHMRC session low risk guideline is a maximum of four standard alcoholic drinks on any day; the Caffeine Energy Drink Use Questionnaire definition of a standard energy drink (ED) was 250ml ED containing approximately 80mg caffeine. BAS Drive and BAS Reward Responsiveness subscale scores ranges from 4-16 and 5-20 respectively, with higher scores indicating greater trait drive and reward sensitivity (Carver & White, 1994) and normative scores for males and females aged 18 to 29 years being 16.8 and 17.6 for Drive and 10.9 and 10.7 for Reward Responsiveness, respectively (Jorm, 1999); I_7 Impulsivity subscale scores range from 0-19, with higher scores indicative of greater rash impulsiveness, and normative scores for males and females aged 16-19 being 9.84 and 9.73 and for males and females aged 20-29 being 7.93 and 9.02 (Eysenck et al., 1985).

Table 2

Mean Outcomes for Breath Alcohol Concentration and the Beverage Rating Scale According to Treatment Condition (N=27)

Outcome	Placebo		Energy Drink		Alcohol		Alcohol and Energy Drink	
	M	***SD***	***M***	***SD***	***M***	***SD***	***M***	***SD***
Breath Alcohol Concentration:								
30 minutes	-	-	-	-	.068	.019	.067	.018
55 minutes (IMT/DMT)	-	-	-	-	.059	.011	.060	.007
75 minutes (CUED)	-	-	-	-	.055	.009	.055	.006
100 minutes (EDT)	-	-	-	-	.045	.009	.046	.007
125 minutes (BRS)	-	-	-	-	.039	.009	.040	.007
Beverage Rating Scale:								
Number of alcoholic drinks	0.3	0.4	0.6	0.8	2.8	1.0	2.9	1.2
Number of standard energy drinks	1.2	0.7	1.0	0.6	1.2	1.1	1.0	0.8

Note. No detectable breath alcohol concentrations were recorded in placebo and energy drink conditions. The Beverage Rating Scale (BRS) range for perceived alcoholic drinks (each drink 4.8% alcohol/volume or 1.4 standard drinks) and standard energy drinks (250ml ED with 80mg caffeine) intake was 0-10 and 0-3, respectively. IMT/DMT: Immediate Memory/Delayed Memory Task; CUED: Cued Go/No-Go task; EDT; Experimental Discounting Task.

Table 3

Multi-Level Linear Model Outcomes for the Primary Behavioural Impulsivity Outcomes

Model[a]	**Alcohol**[b]	**ED**[b]	**Sex**[b]	**Alcohol x ED**[b]	**Alcohol x Sex**[b]	**ED x Sex**[b]	**Alcohol x ED x Sex**[b]
Impulsive Response Initiation:							
Immediate Memory Task: Ratio of commission errors/correction detections[1]	$F_{1, 107.47}$=3.12, p=.080	$F_{1, 107.47}$=0.15, p=.700	-	$F_{1, 107.47}$=0.01, p=.945	-	-	-
Immediate Memory Task: Ratio of commission errors/correction detections[2]	$F_{1, 80.07}$=7.52, p=.008	$F_{1, 80.50}$=0.35, p=.554	$F_{1, 26.85}$=1.82, p=.188	$F_{1, 80.50}$=0.01, p=.914	$F_{1, 80.50}$=1.03, p=.314	$F_{1, 80.50}$=0.15, p=.703	$F_{1, 80.50}$=0.00, p=.984
Delayed Memory Task: Ratio of commission errors/correction detections[1]	$F_{1, 102.79}$=0.05, p=.832	$F_{1, 102.79}$=1.40, p=.240	-	$F_{1, 102.79}$=0.32, p=.575	-	-	-
Delayed Memory Task: Ratio of commission errors/correction detections[2]	$F_{1, 72.19}$=0.13, p=.717	$F_{1, 72.19}$=4.08, p=.047	$F_{1, 26.21}$=.013, p=.726	$F_{1, 102.79}$=0.92, p=.340	$F_{1, 102.79}$=5.90, p=.018	$F_{1, 102.79}$=2.61, p=.111	$F_{1,102.79}$=5.87, p=.018
Response Disinhibition:							
CUED: Proportion valid cued 'no-go' commission errors[1]	$F_{1, 91.61}$=0.08, p=.784	$F_{1, 91.61}$=0.24, p=.629	-	$F_{1, 91.61}$=0.00, p=.948	-	-	-
CUED: Proportion valid cued 'no-go' commission errors[2]	$F_{1, 58.02}$=0.32, p=.574	$F_{1, 58.02}$=0.99, p=.324	$F_{1, 25.12}$=2.03, p=.166	$F_{1, 58.02}$=0.02, p=.893	$F_{1, 58.02}$=6.26, p=.015	$F_{1, 58.02}$=0.09, p=.768	$F_{1, 58.02}$=0.89, p=.350
CUED: Proportion invalid cued 'no-go' commission errors[1]	$F_{1, 101.54}$=0.03, p=.871	$F_{1, 101.54}$=0.22, p=.641	-	$F_{1, 101.54}$=0.04, p=.837	-	-	-
CUED: Proportion invalid cued 'no-go' commission errors[2]	$F_{1, 61.17}$=0.12, p=.735	$F_{1, 61.17}$=0.95, p=.334	$F_{1, 26.56}$=0.46, p=.503	$F_{1, 61.17}$=0.19, p=.669	$F_{1, 61.17}$=2.44, p=.123	$F_{1, 61.17}$=1.78, p=.187	$F_{1, 61.17}$=0.56, p=.458

Table 3 Continued

Model[a]	Alcohol[b]	ED[b]	Sex[b]	Alcohol x ED[b]	Alcohol x Sex[b]	ED x Sex[b]	Alcohol x ED x Sex[b]
Impulsive Decision-Making:							
Experiential Discounting Task: Area under the curve[1]	$F_{1, 88.56}$=0.03, p=.854	$F_{1, 88.56}$=0.25, p=.617	-	$F_{1, 88.56}$=0.46, p=.500	-	-	-
Experiential Discounting Task: Area under the curve[2]	$F_{1, 61.33}$=0.00, p=.969	$F_{1, 60.87}$=1.50, p=.969	$F_{1, 26.11}$=1.35, p=.257	$F_{1, 26.11}$=1.34, p=.252	$F_{1, 26.11}$=1.06, p=.308	$F_{1, 26.11}$=0.84, p=.364	$F_{1, 26.11}$=0.68, p=.413

Note. [a] Those lines indicated with a [1] outline the results of the basic model (fixed factors: Alcohol, ED, Alcohol x ED) and those lines indicated with a [2] outline the results of the adjusted model (fixed factors: Alcohol, ED, Sex, Alcohol x ED, Alcohol x Sex, ED x Sex, Alcohol x ED x Sex; random factor: Subject). [b] These columns outline the main effects and interactions for Mixed Models for Repeated Measures with maximum likelihood estimation and a diagonal covariance structure. ED: energy drink; CUED: Cued Go/No-Go task.

7.5.4 Delayed Memory Task

There were no significant treatment effects for the basic model for DMT ratio (Table 3). The adjusted model showed a significant main effect of ED (p=.047) and a significant interaction of Alcohol x Sex (p=.018); these effects were subsumed by a significant Alcohol x ED x Sex interaction (p=.018) (Figure 2). The model for Active Alcohol showed a trend towards a significant main effect of ED, F(1, 25.36)=3.77, p=.063, and a significant Sex x ED interaction, F(1, 25.36)=6.92, p=.014; there was no significant main effect of Sex (p=.256). Pairwise comparisons revealed that females had a significantly lower DMT ratio after consuming active alcohol with active ED (M=.34, SD=.18) relative to placebo ED (M=.49, SD=.18, p=.007, g=0.82). Males displayed no significant difference in performance according to ED dose after active alcohol (p=.642).

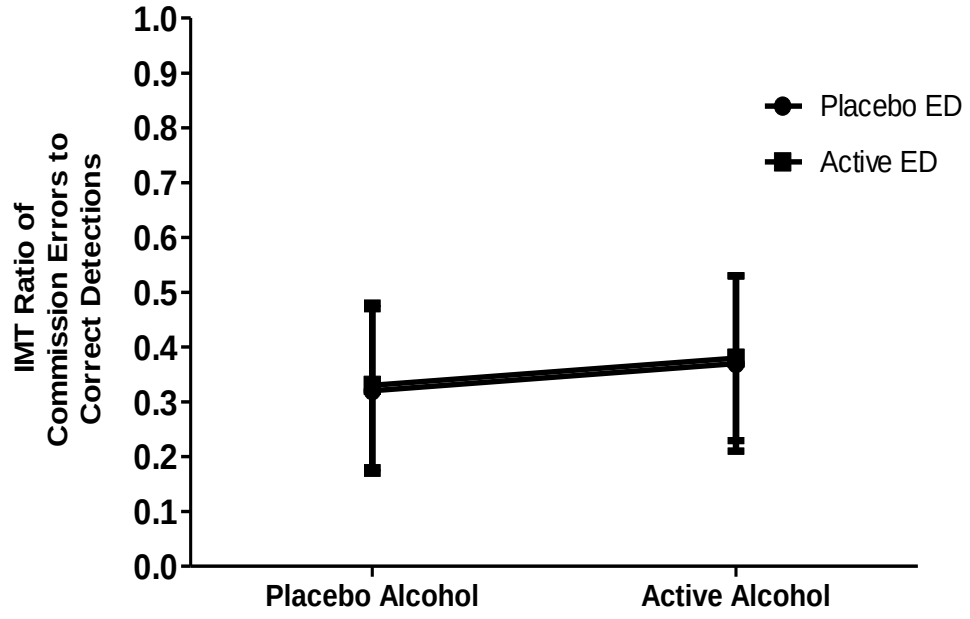

Figure 1. Mean IMT ratio of commission errors to correct detections according to the alcohol and energy drink (ED) dose ingested. The ratio ranges between 0.0 and 1.0, with a higher ratio indicating greater errors relative to correct detections. Error bars represent the standard deviation.

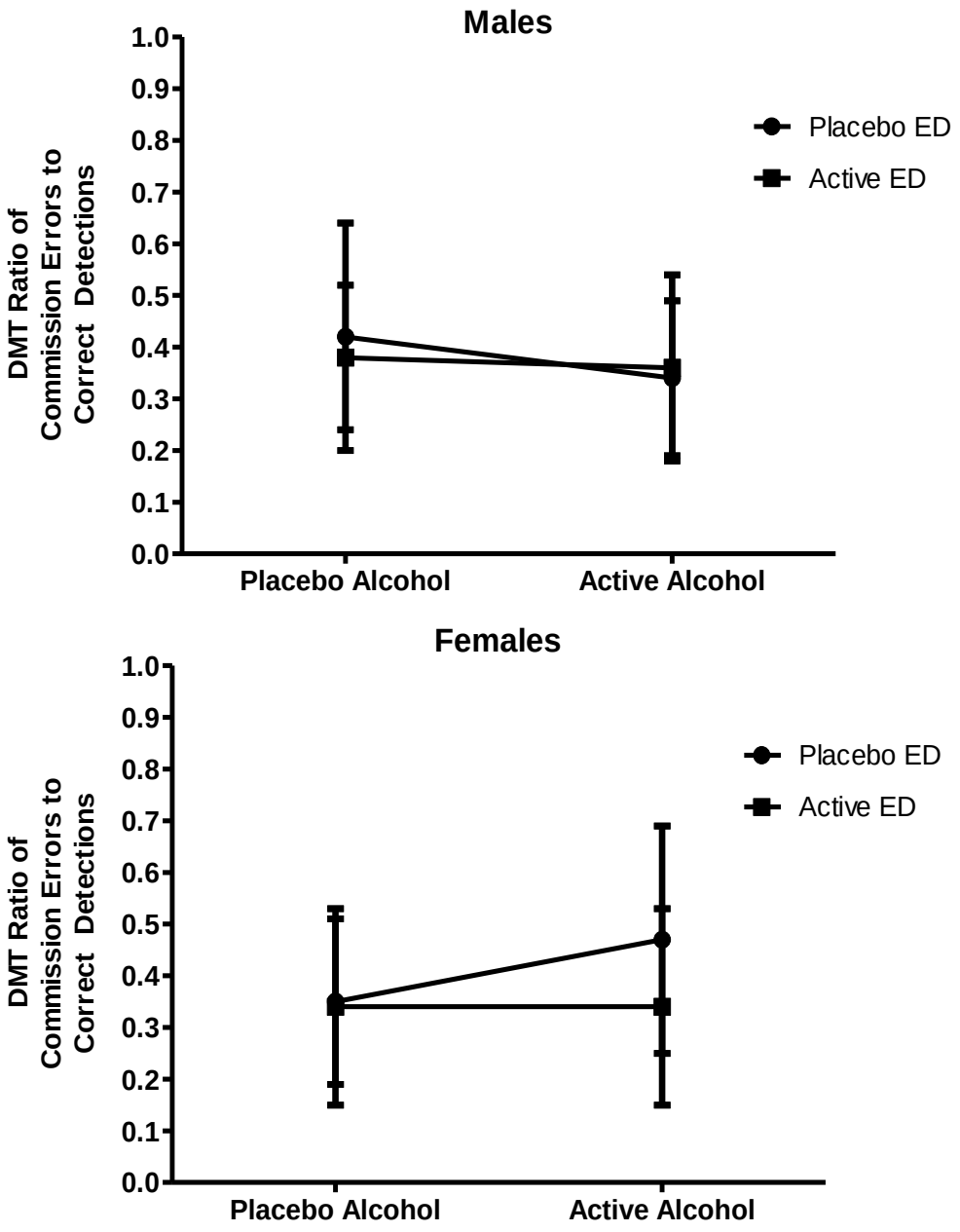

Figure 2. Mean DMT ratio of commission errors to correct detections according to the alcohol and energy drink (ED) dose ingested for males (top panel) and females (bottom panel). The ratio ranges between 0.0 and 1.0, with a higher ratio indicating greater errors relative to correct detections. Error bars represent the standard deviation.

7.5.5 Cued Go/No-Go Task

7.5.5.1 Valid Cued No-Go Targets

There were no significant treatment effects for the basic model (Table 3; Figure 3). The adjusted model showed no significant main effect of Alcohol, ED, or Sex or interaction between these variables, with the exception of a significant Alcohol x Sex interaction (p=.015). Pairwise comparisons showed no significant difference in the proportion of commission errors by males after active or placebo alcohol (p=.176). In contrast, females had a significantly higher proportion of commission errors after active (M=.03, SD=.05) relative to placebo alcohol (M=.01, SD=.05, p=.034, g=0.51). Simple main effects comparisons showed that there was no significant difference in the proportion of commission errors when active alcohol was consumed with placebo ED (M=.03, SD=.04) versus active ED (M=.03, SD=.05, p=.599, g<0.01).

7.5.5.2 Invalid Cued No-Go Targets

There were no significant effects of Alcohol, ED, or Sex for the basic or adjusted model (Table 3; Figure 4). Simple main effects comparison showed no significant change in commission errors when active alcohol was co-ingested with placebo (M=.24, SD=.20) or active ED (M=.23, SD=.26; p=.754, g=0.04).

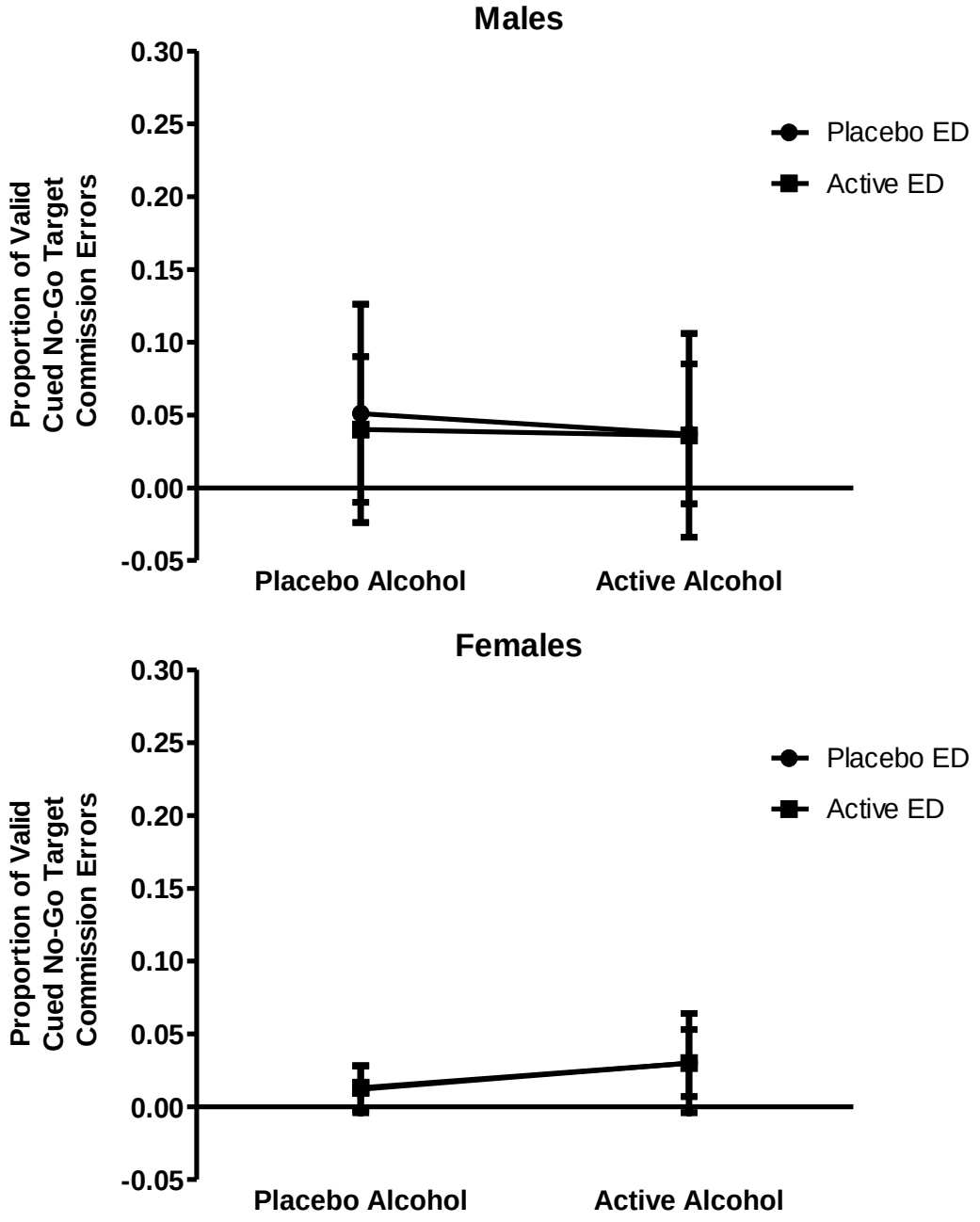

Figure 3. Mean proportion of commission errors to valid cued go targets according to the alcohol and energy drink (ED) dose ingested for males (top panel) and females (bottom panel). The proportion ranges between 0.0 and 1.0, with a higher proportion indicating a greater number of commission errors. Error bars represent the standard deviation.

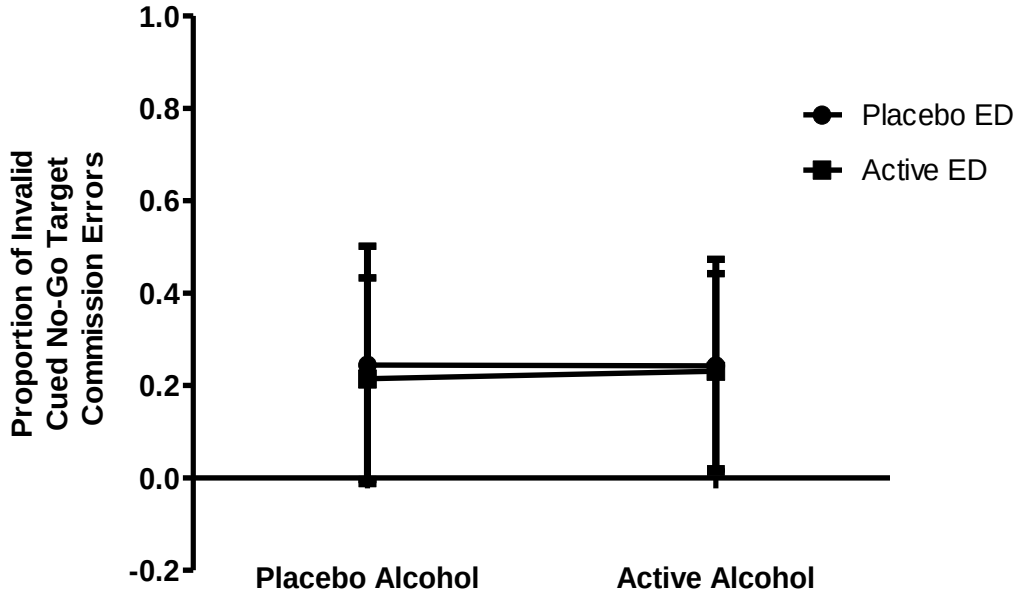

Figure 4. Mean proportion of commission errors to invalid cued go targets according to the alcohol and energy drink (ED) dose ingested. The proportion ranges between 0.0 and 1.0, with a higher proportion indicating a greater number of commission errors. Error bars represent the standard deviation.

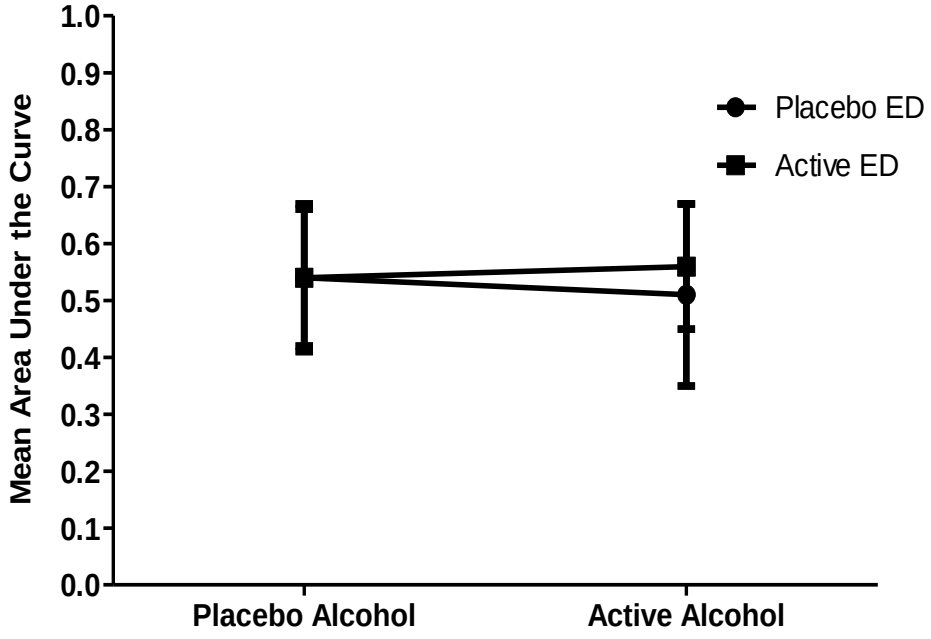

Figure 5. Mean area under the curve according to the alcohol and energy drink (ED) dose ingested. Area under the curve values range between 0.0 and 1.0, with a higher value indicating steeper discounting. Error bars represent the standard deviation.

7.5.6 Experiential Discounting Task

There were no significant effects of Alcohol, ED, or Sex in the basic or adjusted model (Table 3; Figure 5). Simple main effects comparison showed no significant change in area under the curve when active alcohol was co-ingested with placebo (*M*=.48, *SD*=.16) or active ED (*M*=.52, *SD*=.16; *p*=.143, *g*=0.27).

7.5.7 Beverage Rating Scale

Significantly higher alcohol intake (in units of 4.8% alcoholic beverages) was reported in active (*M*=2.9, *SD*=1.0) relative to placebo (*M*=0.50, *SD*=0.49) alcohol conditions, *F(*1,25)=169.83, *p*<.001, *g*=3.13 (Table 2). There was a trend towards a significant main effect of ED, *F(*1,25)=4.02, *p*=.056, *g*=0.36, with participants reporting greater alcohol intake in active ED (*M*=1.8, *SD*=0.8) related to placebo ED (*M*=1.6, *SD*=0.5) conditions. The main effect of Sex was not significant (*p*=.157). However, there was a trend towards a significant Alcohol x Sex interaction, *F(*1,25)=3.74, *p*=.065. Breakdown analyses showed a trend towards greater alcohol intake reported by males (*M*=3.2, *SD*=1.0) relative to females (*M*=2.5, *SD*=0.8) in active alcohol conditions (*p*=.065, *g*=0.77); there were no significant sex differences for placebo alcohol conditions (*p*=.706). No other interactions reached significance (*p*s>.541). Simple main effects comparison revealed no significant difference in reported intake when active alcohol was consumed with active relative to placebo ED (*p*=.509, *g*=0.11).

There was no significant main effect of Alcohol (*p*=.961), ED (*p*=.139), or Sex (*p*=.719), or interaction involving these variables (*p*s>.457) for perceived ED intake. Simple main effects comparison revealed no significant difference in reported intake

when active alcohol was consumed with active relative to placebo ED (p=.393, g=0.16).

7.6 Discussion

The results of the present study indicate that interactive alcohol and ED effects are restricted to behavioural impulsive response initiation, with no statistically significant change in response disinhibition and impulsive decision-making according to whether alcohol was co-ingested with active or placebo ED. The DMT showed a significant reduction in impulsive response initiation when active relative to placebo ED was co-ingested for female participants only, despite no significant difference in BrAC or perceived intoxication. However, this interactive effect of AmED on impulsive response initiation was dependent on task difficulty; alcohol-induced increases in impulsive response initiation were observed on the IMT regardless of whether placebo or active ED was co-ingested. There were generally no treatment effects for response disinhibition, as assessed by the Cued Go/No-Go task, and impulsive decision-making, as assessed by the EDT. The exception was a significant increase in the proportion of commission errors to valid cued 'no-go' targets after active relative to placebo alcohol for female participants only on the Cued Go/No-Go task. This effect occurred regardless of whether active or placebo ED was co-ingested.

These results suggest a differential interactive effect of AmED on behavioural impulsivity, with EDs appreciably attenuating the detrimental effects of alcohol on only one aspect of impulsive behaviour and only under specific conditions (high working memory load for female participants). This is the first study to date to

investigate the effect of AmED on impulsive response initiation; it remains to be seen whether these results are evident at higher doses, and translate to in vivo contexts. In regards to the first point, the current study involved administration of a single ED dose (approximately one 250mL ED per 70kg person). However, a recent survey revealed that AmED consumers ingest between 1 and 10 standard 250mL EDs (*M*=2.4) in their typical AmED sessions, with 33% exceeding the Australian recommended maximum daily intake guidelines and consuming three or more 250mL EDs (Peacock et al., 2012, 2013a). Research extending into these higher dosage domains is necessary to increase the ecological validity of outcomes.

In regards to the second point, an experimental study has shown that AmED administration resulted in small magnitude increases in objectively-measured risk-taking behaviour; this effect was a consequence of ED intake, evident regardless of whether alcohol was co-ingested (Peacock et al., 2013c). In contrast, survey research with AmED consumers has shown lower rates of risk-taking in AmED versus alcohol drinking sessions (de Haan et al., 2012; Peacock et al., 2012, 2013b; Rossheim et al., 2013). This contrast between laboratory-based behaviour and self-reported behaviours in natural drinking contexts means that the role of non-pharmacological factors, such as the drinking environment (Gardner & Steinberg, 2005) and drinking expectancies (B. T. Jones, Corbin, & Fromme, 2001), cannot be discounted. For example, Woolsey et al. (2010) found that AmED consumers had higher expectations of acting aggressively and driving a motor vehicle while under the influence of AmED relative to alcohol. Thus, it may be that other non-pharmacological factors unique to AmED are contributing to differential outcomes when alcohol is consumed alone versus being co-ingested with ED. Expectancy

effects were controlled in the present study by beverage blinding; participants reported equivalent ED intake in AmED versus alcohol conditions. This general paucity of research investigating the effects of AmED impedes evidence-based responses to calls for AmED policy reform (Australian Medical Association, December, 2010), in that we need to determine whether harm reduction endeavours should primarily target the nature of the beverage itself, or expectations of AmED use.

The absence of an interactive alcohol and ED effect and general lack of sensitivity to treatment effects for the measures of response disinhibition and impulsive decision-making may be a consequence of the dosing protocol. The Cued Go/No-Go task, assessing response inhibition, and the EDT, assessing impulsive decision-making, were commenced 75 and 100 minutes after beverage administration when BrAC was descending (BrAC .055% and .046% respectively). In accordance with the present study, Marczinski et al. (2011) recorded no interactive effects of AmED relative to alcohol on response disinhibition. However, Marczinski et al. (2011) found that alcohol increased commission errors relative to placebo, regardless of whether active or placebo ED was co-ingested, and whether the cue was valid or invalid. These results were observed 45 minutes after beverage consumption when BrAC was at peak (BrAC .089%). Similarly, the previous discounting research using operant procedures has only shown an appreciable increase in delay-discounting following administration of high alcohol doses (0.8g/kg; BrAC ~.076% extracted from Figure 1 in Reynolds et al., 2006b) administered 15 and 105 minutes after beverage consumption, with no detectable effect of a low dose (0.4g/kg; BrAC ~.037%). These outcomes suggest that the degree of objective intoxication experienced in the

present study may not have been of a sufficient magnitude at the time of testing to cause a detectable change in response disinhibition and impulsive decision-making. Testing was conducted at this time-point as it is likely that some types of risk-taking (e.g., drink-driving) occur once the consumer has ceased alcohol intake (Fillmore et al., 2008). Previous experimental research has shown acute tolerance in risk-taking following alcohol administration, whereby participants perceive themselves as less intoxicated and report lower sexual risk-taking intentions, on the descending relative to ascending limb (Davis et al., 2009). Future research assessing these outcomes whilst BrAC is ascending, or at peak intoxication, could clarify whether differential interactive effects are evident depending on the BrAC limb.

The methodological characteristics of the response disinhibition and impulsive decision-making tasks may also have contributed to the absence of treatment effects. While it is standard practice to remove anticipatory responses in cognitive research, responses within 200ms of target presentation on the Cued Go/No-Go task were included so as to capture the most extremely premature cued responses. However, the cue-target stimulus onset asynchrony was fixed at 1000ms, thus potentially allowing anticipatory responses. Future research should be undertaken to replicate these results with a variable stimulus-onset-asynchrony. Furthermore, 26% of the sample did not reach an indifference point before the choice-block interval expired on at least one occasion, indicating that some participants never reached a point where they displayed no differential preference for one choice over the other. This failure to reach an indifference point is not uncommon in the delay-discounting literature (e.g., Richards, Sabol, & de Wit, 1999a). However, it is not clear whether this outcome in the present study is a reflection on the amount, delay, and/or

probability of the options. Regardless, these factors should be taken into consideration when drawing conclusions regarding the effect of alcohol, with or without ED, on response disinhibition and impulsive decision-making. The sample size for this study was determined using a priori power calculations based on detecting a practically meaningful effect size (i.e., moderate-to-large magnitude effect; f=0.30). However, given the variability inherent in regards to the effects of alcohol, power for future studies should be calculated accordingly.

In the present study, perceived alcohol intake was significantly greater in the active relative to placebo alcohol conditions, potentially resulting in alcohol expectancy effects. However, perceived intake in the AmED and alcohol conditions did not differ significantly and participants reported alcohol intake in the placebo conditions, suggesting successful placebo manipulation. While ED administration was double-blind, alcohol administration was single-blind, introducing possible experimenter bias. However, systematic procedures were implemented to minimize experimenter bias, including: (i) computerised standardized instructions, (ii) use of objective measurement procedures, and (iii) blinding treatment conditions during data collation and analysis. Finally, it should be considered that the sample comprised normal healthy individuals whose trait impulsivity scores fell below normative levels. The interaction between high trait impulsivity and state-dependent changes in impulsive behaviour requires clarification, particularly as research shows that AmED consumers report heavier drinking patterns and higher trait impulsivity relative to alcohol consumers (e.g., Brache & Stockwell, 2011).

In sum, the present study indicated that differential effects of AmED and alcohol on behavioural impulsivity were restricted to reduction of alcohol-induced impairment of impulsive response initiation following ED co-ingestion (although this effect was only evident for female participants when task difficulty was elevated). However, the general absence of alcohol treatment effects for response disinhibition and impulsive decision-making suggests that the magnitude of the effects may not have been sufficient for detection using the administered tasks. Research adopting more complex dosing protocols involving higher ED doses is required to determine whether the absence of interactive AmED effects is a function of methodology or reflects genuine equivalence in behavioural impulsivity.

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Chapter 8: 'High' Intoxication: The Effect of Alcohol and Energy Drink Co-Ingestion on Objective and Subjective Intoxication

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8.1 Preface

This chapter outlines the results from an experimental study (*Study 3*) assessing the dose-dependent effects of alcohol and ED on objective and subjective intoxication outcomes. In accordance with the existing literature, the experimental research outlined in *Chapters 5*, *6*, and *7* typically yielded no detectable interactive effects of AmED relative to alcohol alone on actual and perceived intoxication. However, this research, and all previous experimental AmED research (with the exception of Alford et al., 2012), has involved administration of a single low ED dose, despite reports that consumers typically ingest twice this amount. The manuscript in the current chapter outlines the results of a dose-dependent experimental study (*Study 3*) undertaken to determine whether the interactive effects of alcohol and ED on actual and perceived intoxication differ according to the amount of alcohol and ED dose co-administered (*Question 6.1* and *6.2*). This study provides an evidence base regarding the potential effects of matching or exceeding the current recommended maximum ED intake guidelines in Australia when at a level of intoxication similar to the legal BAC driving limits in Australia and in the United States. The results could inform public health initiatives aimed at facilitating consumer awareness and education regarding AmED-induced changes in intoxication and the potential ramifications of this altered state of inebriation.

8.2 Abstract

Background: Alcohol mixers with high sugar content are associated with lower breath alcohol concentration (BrAC). It is theorised that consuming alcohol mixed with energy drinks (AmED) causes underestimation of intoxication. However, there is a dearth of research assessing dose-dependent interactions to determine whether mixing energy drinks (EDs) with alcohol alters BrAC and, if so, whether perceived intoxication ratings reflect these changes.

Methods: Using a single-blind, placebo-controlled, mixed design, 30 participants (15 males) were assigned to an alcohol treatment group (placebo, moderate BrAC ~.050%; high BrAC ~.080%) and attended four sessions in which they were co-administered: (i) 0mL ED (placebo), (ii) 250mL ED, (iii) 500mL ED, and (iv) 750mL ED; beverage volume was consistent across sessions. BrAC and perceived intoxication were assessed at 30 and 170 minutes post-administration.

Results: BrAC was lower after AmED relative to alcohol, with significant large magnitude decrements after the same alcohol dose was co-administered with 500mL ED and 750mL ED relative to 0mL ED. Whilst generally not reaching statistical significance, there were moderate-to-large magnitude decreases in perceived intoxication ratings when the moderate alcohol dose was co-administered with 750mL ED relative to alcohol with 0mL, 250mL or 500mL ED after controlling for BrAC differences.

Conclusions: Objective intoxication was lower after consuming AmED relative to alcohol alone. While not statistically significant, moderate effect sizes indicated that co-ingesting alcohol and EDs may result in lower intoxication ratings even after controlling for BrAC, with important implications for alcohol consumption levels and engagement in risk taking.

8.3 Introduction

The practice of consuming alcohol mixed with energy drinks (AmED) has generated considerable concern amongst researchers (Pennay & Lubman, 2012b; Weldy, 2010), health professionals (Australian Medical Association, December, 2012, January, 2013), and regulatory bodies (Food Safety Promotion Board; Food Standards Australia and New Zealand, 2001; United States Food and Drug Administration, November, 2010). Energy drinks (EDs) are beverages marketed as improving performance by reversing fatigue and increasing alertness (Heckman et al., 2010). Caffeine is the main ingredient thought to produce behavioural effects (Nordt et al., 2012), with a maximum content of 320mg/L in Australia (80mg per standard 250ml beverage) (Food Standards Australia and New Zealand, 2009). AmED consumption has been theorised to create a state of 'wide-awake drunkenness' (Arria & O'Brien, 2011), whereby the stimulatory nature of the ED masks the depressant effects of alcohol which act as a subjective indicator of intoxication. Consequently, it is theorised that AmED consumers may report lower intoxication relative to when consuming an equivalent quantity of alcohol without ED. This misperception of intoxication may result in poorer decision making and heighten the risk of alcohol-related harm (Ferreira et al., 2006; Weldy, 2010).

Early experimental research by Ferreira et al. (2006) is often cited as the primary evidence for this hypothesis. In this study, participants recorded significantly reduced ratings on three indices of intoxication ('headache' at 30 minutes and 'dry mouth' and 'alterations in motor coordination' at 120 minutes) after consuming alcohol (0.6g/kg or 1.0g/kg) with 3.57mL/kg ED compared to when co-ingesting placebo ED. No differential treatment effects were recorded on other indices of

intoxication (e.g., tiredness, dizziness, and nausea). Subsequent double-blind, placebo-controlled experimental research utilising perceived alcohol intake as an index of subjective intoxication have revealed similar outcomes when alcohol (mean peak BrAC .043% -.089%) is consumed alone or with ED (1.82mL/kg to 3.57mL/kg) (Marczinski et al., 2011; Marczinski et al., 2012, 2013). Only one experimental study (Peacock et al., 2013c) has included a direct assessment of level of intoxication, revealing no statistically significant differences in ratings of perceived intoxication, or perceived alcohol intake, after alcohol (mean peak BrAC .068%) was administered alone or in combination with 3.57mL/kg ED.

Thus, the existing body of experimental research generally contradicts the hypothesis of AmED-induced reduced perception of intoxication. However, it may be that the effect of AmED on perceived intoxication is dose-dependent. The previous experimental research has involved administration of between 125mL and 250mL ED (40 to 80mg caffeine) per 70kg person (Ferreira et al., 2006; Marczinski et al., 2011; Marczinski et al., 2012, 2013; Peacock et al., 2013c). In contrast, AmED consumers report ingesting between two and three standard 250mL EDs in a typical drinking session (Peacock et al., 2012; Woolsey et al., 2010). As such, research assessing the dose-dependent effects of AmED and extending into higher ED dosage domains is necessary to increase ecological validity and determine whether interactive effects become apparent following greater intake.

This lack of dose-dependent research also has implications for conclusions regarding the effect of AmED on objective intoxication. Previous research has shown that alcohol absorption is impacted by the speed of gastric emptying (Oneta et al., 1998),

with the presence of food delaying emptying of the stomach, decreasing alcohol absorption, and reducing BAC. Following from this, it has been established that alcohol mixer beverage composition may impact on gastric emptying: specifically, those mixers which contain natural sugars have a slower rate of gastric emptying, slowing the rate of absorption and decreasing peak blood ethanol concentration (Wu et al., 2006).

While increased carbohydrate content of alcohol mixers may decrease BrAC, consumers may remain unaware of these differences in actual intoxication. A double-blind, placebo-controlled, parallel experimental study showed that, as predicted, BrAC was lower after ingesting the same alcohol dose (1.97mL/kg) with a natural (peak mean BrAC .077%), as opposed to an artificial, sweetened mixer (peak mean BrAC .091%). However, participants reported equivalent ratings of intoxication, despite the disparity in objective intoxication (Marczinski & Stamates, 2013). It is important to note that perceived intoxication ratings were not adjusted for BrAC despite the magnitude of the decrease in BrAC after natural versus artificially sweetened mixer.

To date, there has been no investigation as to whether an increasing dose of naturally sweetened ED decreases BrAC, and whether such changes impact on perceived intoxication when ingesting AmED at the higher quantities consumed in the night-time economy. There has been one study using a multi-dose design, adopting staggered administration of two 250mL ED doses. This study showed no statistically significant difference in objective intoxication outcomes after AmED relative to alcohol, however the natural sugar content of placebo additions (peppermint syrup

and apple and blackcurrant concentrate) was not stated (Alford et al., 2012). As such, the aim of the present study was to determine the dose-dependent effect of co-ingesting alcohol and ED on objective and subjective intoxication.

8.4 Method

8.4.1 Design

This was a placebo-controlled, single-blind, mixed design study. Participants were randomly assigned a treatment code counterbalanced for sex corresponding to an alcohol group assignment (placebo, moderate, or high alcohol group) and counterbalanced ED treatment administration order (0mL (*placebo*), 250mL, 500mL, and 750mL ED dose). While the participant, data collector, and data analyst were blind to ED administration, only the former was blind to alcohol administration.

8.4.2 Participants

The sample comprised 30 healthy volunteers (15 males) aged between 20 and 35 years assigned to three groups (n=10; 5 males per group). Participants were self-reported regular ED, caffeine, and alcohol consumers, as indicated by consumption of: (i) at least one ED in the past month, with intake not exceeding one ED per day on average, (ii) between 5 and 28 caffeinated products in the preceding week, and (iii) at least two standard alcoholic drinks in the preceding fortnight. All participants reported English as a first language, attainment of secondary school education, normal sleep patterns, and normal or corrected-to-normal vision. Additional exclusion criteria pertained to: (i) current pregnancy or lactation, (ii) significant medical condition, (iii) current significant psychiatric disorder or Kessler

Psychological Distress Scale (K10; Kessler et al., 2002) score of ≥30, (iv) history of a drug use or Alcohol Use Disorders Identification Test (AUDIT; Babor et al., 2001) score of ≥16, (v) significant intellectual disability or Wechsler Test of Adult Reading (WTAR) IQ of ≤70, and (vi) current regular tobacco or prescription medication use, or illicit drug use (preceding six months).

Participants were recruited via noticeboard advertisements and print and radio media reports. The research protocol was approved by the Human Research Ethics Committee Tasmania Network. Informed consent was provided prior participation. Participants were advised they may receive alcohol (maximum approximately six standard drinks) and EDs (maximum approximately three standard 250ml serves) during some or all of the sessions. Participants received an honorarium of 40 AUD per experimental session.

8.4.3 Materials

8.4.3.1 Alcohol, Caffeine, and Energy Drink Intake Measures

The Timeline Follow-Back (TLFB; Sobell & Sobell, 1992) questionnaire assessed daily standard alcoholic drink intake for the preceding 30 days. A Caffeine and Energy Drink Use Questionnaire measured self-reported average daily caffeine intake (mg) and past month ED use.

8.4.3.2 Trait Impulsivity Measures

Rash impulsivity was assessed via the I_7 Impulsiveness subscale (Eysenck et al., 1985), a 19 item scale with a yes/no response format.

8.4.3.3 Subjective Measures

Participants rated their subjective level of intoxication on a 100-mm visual analogue scale (Peacock et al., 2013c); anchors were designated 'not at all' and 'very much'. A Beverage Rating Scale (BRS; Fillmore & Vogel-Sprott, 2000) assessed perceived alcohol intake (bottles of beer containing 4.8% alcohol; scale range 0 to 10, increments of 0.5) and number of standard 250mL EDs containing 80mg caffeine (scale range 0 to 3; increments of 0.5) consumed during beverage administration.

8.4.4 Treatment Conditions

Alcohol doses were determined by body weight. The moderate and high alcohol groups received 0.50g/kg and 0.65g/kg vodka (37.5% a/v Smirnoff Red Label No. 21 vodka), respectively. The dose was reduced to 85% for females, with an intended peak BrAC of .050% (Australian legal drink driving limit) and .080% (United States legal drink driving limit). The placebo alcohol group received 3ml vodka floated on each beverage portion, with a light alcohol mist sprayed over the beverage container.

Three ED conditions comprised active ED doses: (i) one standard 250mL ED, (ii) two standard 250mL EDs, and (iii) three standard 250mL EDs. The ED contained 80mg caffeine, 1000mg taurine, 60mg glucuronolactone, and 27g sugar per 250mL portion. The fourth ED condition comprised a placebo ED dose of 750mL soda water. Adopting a similar placebo design as Alford et al. (2012), all ED doses were supplemented with Torani® sugar-free English Toffee and Black Cherry syrups to match the taste, appearance, and smell of the beverages, and soda water supplementation ensured consistent beverage volume. The active constituents were

chosen based on endorsement as the most popular AmED mixers in a recent consumer survey (Peacock et al., 2012).

8.4.5 Procedure

Participants attended one 60-minute familiarisation session and four 270-minute experimental sessions. Sessions commenced between 8:00am and 5:00pm (85% of sessions commenced at 9am or 1pm), with a minimum of two and maximum of 14 days separating sessions. With the exception of a standard breakfast bar consumed 90 minutes prior, participants fasted for 4 hours before each session (a prior standard light meal was advised) and abstained from caffeine for 8 hours, alcohol and medication (excluding contraceptives) for 24 hours, and illicit drugs for the study duration.

Zero BrAC was verified using an Alcolizer HH-2 breathalyser (Alcolizer Pty Ltd.) prior to session commencement. Participants were administered the beverage in three portions served in opaque lidded cups, consuming each portion at a steady pace over a five minute period. Participants were breathalysed and completed the subjective intoxication measures at 30 minutes and 170 minutes after commencing beverage administration, with companion study experimental tasks completed in the interval. At the end of testing, participants received a detoxification meal and remained in the laboratory until recording two BrAC measurements of ≤0.03% within 15 minutes.

8.4.6 Data Analysis

Missing data due to technical malfunction resulted in a smaller dataset for BrAC (30 minutes: *N*=28) and the BRS (*N*=29). Change scores from baseline were calculated

for subjective intoxication. Mixed Models for Repeated Measures (MMRM) analysis using maximum likelihood estimation with a diagonal covariance structure were conducted using IBM SPSS Statistics version 21. The basic model tested comprised Alcohol (Placebo, Moderate, High), ED (0mL (placebo), 250mL, 500mL, and 750mL) and Alcohol x ED as fixed factors; the placebo alcohol condition was removed for BrAC analyses. The adjusted model also included Subject as a random factor and Sex (Male, Female), Alcohol x Sex, ED x Sex, and Alcohol x ED x Sex as fixed factors; sample characteristics registering significant group differences were included as a covariate. Significant main effects or interactions including Alcohol and/or ED which reached traditional significance (p<.050) were followed up by pairwise comparisons to determine the effect of ED within each alcohol dose; false discovery rate (Benjamini & Hochberg, 1995) controlled for error rates. The study was powered on the basis that the chosen sample size (N=30) would allow reliable (power = 0.80) detection of an alcohol-ED interactive effect of moderate magnitude (Cohen's d =0.50) as statistically significant (α= 0.05); an effect smaller than this would be unlikely to have a meaningful impact on behaviour. As there was low power for individual comparisons, effect sizes (Hedges' g; Hedges, 1981) were calculated for pairwise follow-up tests, with those identified as of moderate (g≥0.50) or large (g≥0.80) magnitude discussed as meaningful regardless of statistical significance. MMRM models were run separately for BrAC and perceived intoxication ratings at 30 and 170 minutes in order to examine outcomes on the ascending and descending BrAC limbs separately.

8.5 Results

8.5.1 Sample Characteristics

There were no significant differences amongst the groups for each demographic, caffeine use, and alcohol use outcome, with the exception of TLFB alcohol intake frequency (Table 1). The moderate alcohol group consumed alcohol significantly more frequently than the placebo alcohol group, $t(18)=-3.02$, $p=.007$, with no significant difference in alcohol intake frequency for the placebo and high alcohol group ($p=.153$) or the moderate and high alcohol group ($p=.173$). There was no significant group difference in regards to AUDIT scores, suggesting that this difference in drinking days did not translate into greater levels of harmful alcohol use by one experimental group.

8.5.2 Post-Administration: 30 Minutes

8.5.2.1 Breath Alcohol Concentration

The basic model showed a significant main effect of ED and a trend towards a main effect of Alcohol for BrAC at 30 minutes; the Alcohol x ED interaction failed to reach significance (Table 2). For the adjusted model, there was a trend towards a main effect of Alcohol as expected, with a large magnitude increase in BrAC in the high alcohol group ($M=.063$, $SD=.009$) relative to the moderate alcohol group ($M=.055$, $SD=.009$, $g=0.89$). There was also a significant main effect of ED; no other treatment effects reached statistical significance (Figure 1). Pairwise comparisons showed a significant large magnitude decrease in BrAC after 750mL ED ($M=.049$, $SD=.006$) compared to 0ml ($M=.068$, $SD=.009$, $p<.001$, $g=2.99$), 250mL ($M=.064$, $SD=.009$, $p=.001$, $g=1.78$), and 500mL ($M=.056$, $SD=.010$, $p=.183$, $g=0.94$) ED; the

final comparison did not reach statistical significance. There was also a significant large magnitude decrease in BrAC after 500mL ED compared to 0mL (p=.020, g=1.39) and 250mL (p=.243, g=0.82) ED; again, the latter comparison was not statistically significant. The difference in BrAC after 250mL ED relative to 0mL ED was of small magnitude (p=0.99, g=0.43).

8.5.2.2 Perceived Intoxication Rating

The basic model showed a significant main effect of Alcohol for perceived intoxication ratings at 30 minutes; the main effect of ED and the Alcohol x ED interaction did not reach statistical significance (Table 2). In the adjusted model, there were significant main effects of Alcohol and ED, with no significant main effect of Sex and no significant interactions (Figure 1). For the former effect, there was a large magnitude increase in intoxication ratings in the high (M=49.6, SD=17.0) relative to the placebo (M=13.19, SD=18.2, p<.001, g=2.07) and moderate (M=30.17, SD=18.4, p=.060, g=1.10) alcohol groups, with the moderate alcohol group also recording a large magnitude increase in intoxication ratings relative to the placebo alcohol group (p=.181, g=0.93); the final two comparisons did not reach statistical significance.

Table 1

Demographic Characteristics, Personality, and Self-Reported Alcohol, Caffeine and ED Use and Baseline Subjective Intoxication Outcomes According to Alcohol Treatment Group (Standard Deviation in Parentheses)

Outcome	**Overall Sample (*N*=30) *M* (*SD*)**	**Placebo Alcohol Group (*n*=10) *M* (*SD*)**	**Moderate Alcohol Group (*n*=10) *M* (*SD*)**	**High Alcohol Group (*n*=10) *M* (*SD*)**	**Statistics**	
					F	***p***
Age (years)	24.7 (3.4)	23.6 (3.3)	25.4 (3.4)	25.0 (3.7)	0.743	.485
Weight (kg)	78.07 (27.0)	80.4 (21.8)	68.5 (12.0)	88.1 (40.3)	1.306	.288
Intellectual functioning (WTAR)	108.2 (10.8)	104.2 (9.9)	108.5 (11.0)	112.0 (11.0)	1.346	.277
Psychological distress (K10 score)	12.9 (2.9)	13.3 (3.9)	11.7 (1.6)	13.8 (2.6)	1.478	.246
Trait impulsivity (I_7 score)	6.7 (3.4)	7.7 (3.6)	6.7 (3.9)	5.8 (2.7)	0.782	.467
Harmful alcohol use (AUDIT score)	7.2 (3.3)	7.8 (4.2)	6.3 (1.6)	7.4 (3.7)	0.525	.597
TLLFB Alcohol Use (past month):						
Days any alcohol	10.8 (5.3)	7.8 (2.7)	14.0 (5.9)	10.5 (5.1)	4.277	.024
Days exceed NHMRC lifetime low-risk guideline	7.0 (4.3)	5.0 (1.7)	8.8 (5.8)	7.1 (3.8)	2.124	.139
Days exceed NHMRC session low-risk guideline	4.9 (4.0)	3.1 (2.2)	6.6 (5.5)	5.0 (3.2)	2.066	.146
Average standard alcoholic drinks per drinking day	5.6 (2.6)	5.3 (2.7)	6.0 (3.1)	5.6 (2.0)	0.169	.846
Maximum standard alcoholic drinks per drinking day	12.8 (7.6)	9.8 (4.8)	15.0 (10.0)	13.3 (6.4)	1.182	.323

Table 1 Continued

	Overall Sample (*N*=30) *M* (*SD*)	**Placebo Alcohol Group (*n*=30) *M* (*SD*)**	**Moderate Alcohol Group (*n*=30) *M* (*SD*)**	**High Alcohol Group (*n*=30) *M* (*SD*)**	**Statistics**	
					F	***p***
Caffeine/Energy Drink Use:						
Average daily caffeine intake (mg)	277.2 (166.7)	341.0 (176.3)	230.4 (107.4)	260.1 (199.2)	1.195	.318
Average standard EDs per drinking day (past month)	1.4 (0.7)	1.3 (0.7)	1.2 (0.4)	1.6 (0.8)	0.967	.393
Maximum standard EDs per drinking day (past month)	2.4 (.7)	2.6 (1.2)	2.9 (2.6)	1.7 (0.8)	1.314	.285

Note. Wechsler Test of Adult Reading (WTAR) standardised score is 100, with higher scores indicative of higher levels of general pre-morbid intellectual functioning; Kessler Psychological Distress Scale (K10; Kessler et al., 2002) score range is 10-50, with scores of 30 or higher indicative of a moderate to severe psychological distress; I_7 Impulsivity subscale scores range from 0-19, with higher scores indicative of greater rash impulsiveness, and normative scores for males and females aged 16-19 being 9.84 and 9.73 and for males and females aged 20-29 being 7.93 and 9.02 (Eysenck et al., 1985); Alcohol Use Disorders Identification Test (AUDIT; Babor et al., 2001) score range is 0-40, with a score of 16 or more indicative of hazardous or harmful alcohol use; the Timeline Follow Back (TLFBSobell & Sobell, 1992) reflects participants' alcohol consumption in the preceding month; National Health and Medical Research Council (NHMRC; 2009) lifetime low risk guideline is a maximum of two standard alcoholic drinks on any day; NHMRC session low risk guideline is a maximum of four standard alcoholic drinks on any day; the Caffeine Energy Drink Use Questionnaire definition of a standard energy drink (ED) was 250ml ED containing approximately 80mg caffeine.

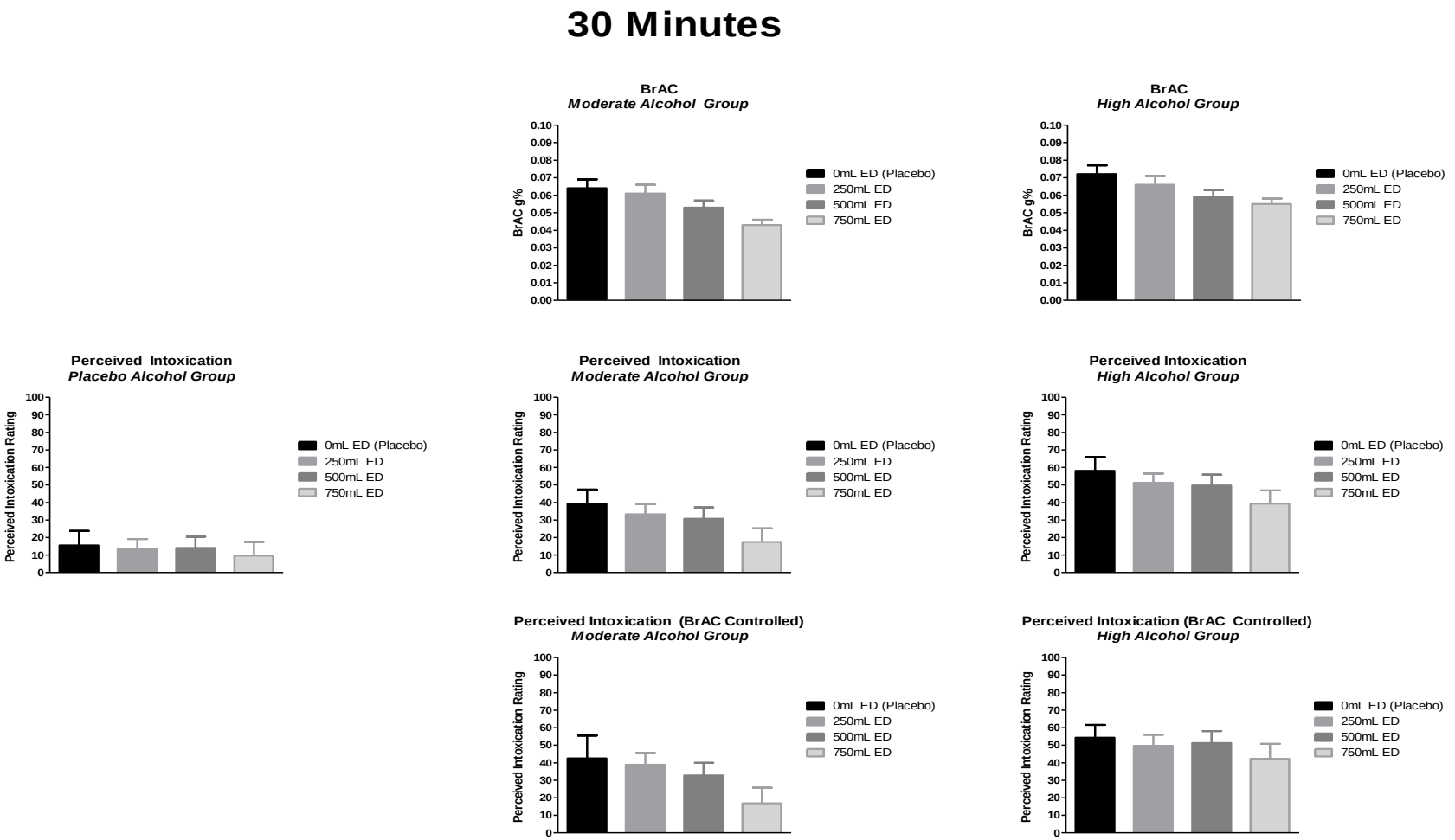

Figure 1. Mean breath alcohol concentration (BrAC) and perceived intoxication ratings at 30 minutes for each alcohol group according to the volume of energy drink co-ingested. Perceived intoxication ratings depicted here reflect the change from baseline; ratings ranged from 0-100. An increased change score indicates greater perception of intoxication. Error bars depict the standard error.

As the main effect of ED on perceived intoxication could reflect BrAC differences, a basic MMRM (with Subject as a random factor) was run for each active alcohol group including BrAC at the time of testing as a covariate. The main effect of ED was not significant in the model for the high alcohol group (p=.518; Figure 1). In contrast, the main effect of ED reached statistical significance in the model for the moderate alcohol group, $F(3,15)=4.44$, p=.021 (Figure 1). There were moderate-to-large magnitude decreases in perceived intoxication ratings after 750mL ED (M=16.8, SD=28.0) relative to 0mL (M=42.5, SD=30.0, p=.397, g=0.76), 250mL (M=38.8, SD=20.2, p=.022, g=1.06), and 500mL (M=32.7, SD=22.9, p=.150, g=0.63) ED; the first and last comparison did not reach statistical significance. Large magnitude decreases in perceived intoxication ratings were also observed after 500mL relative to 250mL ED (p=.592, g=1.26). No other pairwise comparisons differed significantly (ps=0.99) with meaningful effect sizes (g=0.15 to 0.32).

8.5.3 Post-Administration: 170 Minutes

8.5.3.1 Breath Alcohol Concentration

The basic model showed a significant main effect of Alcohol for BrAC at 170 minutes; the main effect of ED and the Alcohol x ED interaction were not significant (Table 2). In the adjusted model, there were significant main effects of Alcohol, ED, and Sex; no interactions reached significance (Figure 2). For the Alcohol main effect, BrAC was significantly lower in the moderate (M=.025, SD=.010) relative to the high (M=.049, SD=.010, g=2.40) alcohol group. For the ED main effect, there was a significant large magnitude decrease in BrAC after 750mL ED (M=.033, SD=.011) relative to 0mL (M=.042, SD=.010, p=.001, g=1.70) and 250mL (M=.039, SD=.010, p=.016, g=1.20) ED, with only a non-significant small magnitude

difference relative to BrAC after 500mL ED (*M*=.034, *SD*=.011, *p*=0.99, *g*=0.16). There was a large magnitude decrease in BrAC after 500mL relative to 0mL (*p*=.001, *g*=1.15) and 250mL (*p*=.060, *g*=1.03) ED; only the former effect reached statistical significance. While not statistically significant, there was also a moderate magnitude decrease in BrAC after 250mL relative to 0mL ED (*p*=.237, *g*=0.66)

8.5.3.2 Subjective Intoxication Rating

The basic model showed a significant main effect of Alcohol for perceived intoxication ratings at 170 minutes; the main effect of ED and interaction between Alcohol and ED were not significant (Table 2). Only the main effect of Alcohol was significant in the adjusted model (Figure 2). There was a large magnitude increase in perceived intoxication ratings in the high (*M*=36.0, *SD*=18.3) relative to the placebo (*M*=6.1, *SD*=19.7, *p*=.004, *g*=1.57) and moderate (*M*=16.4, *SD*=19.9, *p*=.093, *g*=1.03) alcohol groups and, in turn, a moderate magnitude increase in the moderate relative to placebo alcohol group (*p*=.867, *g*=0.52); the final two comparisons did not reach statistical significance.

The MMRM model was run again for each active alcohol group including BrAC at the time of testing as a covariate to determine if differences were apparent after controlling for BrAC. There was no significant main effect of ED for the moderate (*p*=.447) or high (*p*=.627) alcohol group (Figure 2), suggesting that there was no ED-induced difference in perceived intoxication after controlling for BrAC.

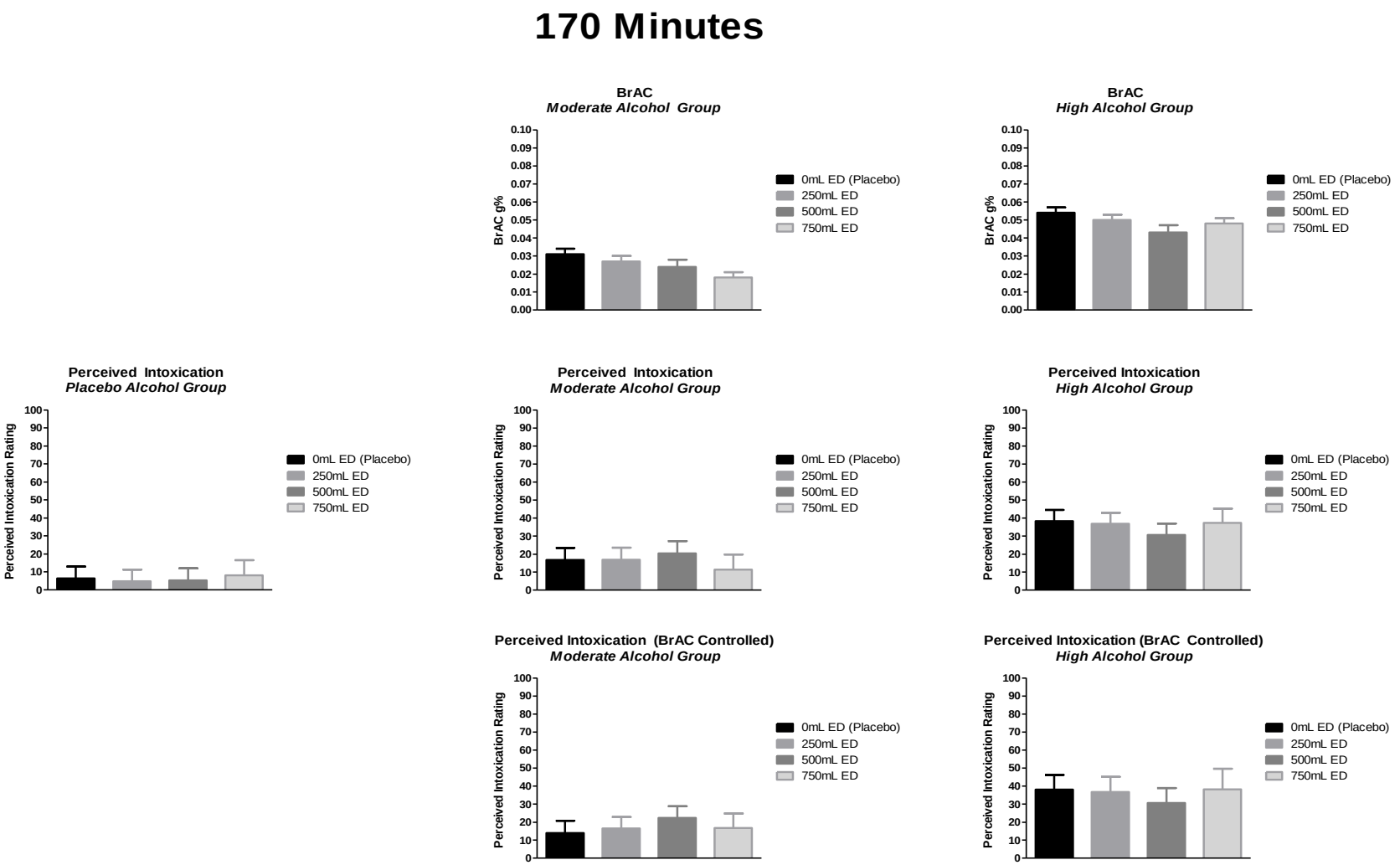

Figure 2. Mean breath alcohol concentration (BrAC) and perceived intoxication ratings at 170 minutes for each alcohol group according to the volume of energy drink co-ingested. Perceived intoxication ratings depicted here reflect the change from baseline; ratings ranged from 0-100. An increased change score indicates greater perception of intoxication. Error bars depict the standard error.

Table 2

Multi-Level Linear Model Outcomes for Objective Intoxication (Breath Alcohol Concentration) and Subjective Intoxication at 30 and 170 Minutes

Model[a]	**Alcohol**[b]	**ED**[b]	**Sex**[b]	**Alcohol x ED**[b]	**Alcohol x Sex**[b]	**ED x Sex**[b]	**Alcohol x ED x Sex**[b]	**TLFB Frequency**[b]
BrAC 30 minutes[1]	$F_{1, 64.77}$=3.99, p=.050	$F_{3,47.43}$= 6.99, p<.001	-	$F_{3,47.43}$=0.27, p=.844	-	-	-	-
BrAC 30 minutes[2]	$F_{1,24.13}$=3.42, p=.077	$F_{3,29.62}$= 14.14, p<.001	$F_{1,24.27}$= 13.24, p=.001	$F_{3,29.62}$=0.49, p=.689	$F_{1,24.54}$=3.80, p=.063	$F_{3,29.62}$=1.11, p=.361	$F_{3,29.62}$=0.77, p=.519	$F_{1,19.57}$= 0.13, p=.911
BrAC 170 minutes[1]	$F_{1,78.26}$=87.30, p<.001	$F_{3,37.38}$=2.81, p=.053	-	$F_{3,37.38}$=0.67, p=.577	-	-	-	-
BrAC 170 minutes[2]	$F_{1, 19.70}$=30.61, p<.001	$F_{3,24.45}$= 10.48, p<.001	$F_{1,19.70}$=7.58, p=.012	$F_{3,24.45}$=2.41, p=.092	$F_{1,19.73}$=0.02, p=.886	$F_{3,24.45}$=0.66, p=.588	$F_{3,24.45}$=1.09, p=.372	$F_{1,19.33}$= 0.64, p=.434
Subjective Intoxication 30 minutes [3]	$F_{2,111.06}$=29.20, p<.001	$F_{3,58.40}$=2.18, p=.100	-	$F_{6,58.4}$=0.23, p=.967	-	-	-	-
Subjective Intoxication 30 minutes[4]	$F_{2,34.65}$=11.04, p<.001	$F_{3,36.58}$=3.87, p=.017	$F_{1,35.07}$=0.32, p=.576	$F_{6,36.58}$=0.43, p=.852	$F_{2,35.09}$=1.32, p=.280	$F_{2,6.58}$=0.73, p=.542	$F_{6,36.58}$=1.25, p=.304	$F_{1,29.82}$=1.64, p=.210
Subjective Intoxication 170 minutes[3]	$F_{2,115.50}$=22.43, p<.001	$F_{3,57.24}$=0.03, p=.992	-	$F_{6,57.24}$=0.35, p=.908	-	-	-	-
Subjective Intoxication 170 minutes[4]	$F_{2,29.68}$=6.70, p=.004	$F_{3,26.10}$=0.16, p=.921	$F_{1,29.82}$=0.72, p=.404	$F_{6,26.10}$=0.96, p=.470	$F_{2,29.82}$=0.33, p=.723	$F_{3,26.10}$=1.71, p=.190	$F_{6,26.10}$=1.25, p=.315	$F_{1,28.28}$=0.46, p=.705

Table 2 Continued

Model[a]	Alcohol[b]	ED[b]	Sex[b]	Alcohol x ED[b]	Alcohol x Sex[b]	ED x Sex[b]	Alcohol x ED x Sex[b]	TLFB Frequency[b]
BRS Number of Alcoholic Drinks[3]	$F_{2,114.89}$=8.48, p<.001	$F_{3,57.88}$=1.16, p=.334	-	$F_{6,57.92}$=0.42, p=.864	-	-	-	-
BRS Number of Alcoholic Drinks[4]	$F_{2,27.98}$=8.41, p=.001	$F_{3,43.73}$=1.63, p=.197	$F_{1,27.92}$=3.23, p=.083	$F_{6,43.77}$=0.58, p=.748	$F_{2,27.68}$=1.37, p=.270	$F_{3,43.73}$=1.60, p=.203	$F_{6,43.77}$=0.76, p=.608	$F_{1,28.23}$=5.44, p=.027
BRS Number of EDs[3]	$F_{2,100.18}$=3.99, p=.021	$F_{3,67.82}$=5.29, p=.002	-	$F_{6,67.85}$=0.71, p=.640	-	-	-	-
BRS Number of EDs[4]	$F_{2,106.43}$=3.17, p=.046	$F_{3,66.68}$=5.90, p=.001	$F_{1,102.42}$=0.37, p=.691	$F_{6,66.73}$=0.79, p=.585	$F_{2,102.42}$=0.37, p=.691	$F_{3,66.68}$=0.98, p=.407	$F_{6,66.73}$=1.54, p=.179	$F_{1,105.40}$=0.02, p=.882

Note. [a] [1] This line details the outcomes from the basic model for BrAC with Alcohol (Moderate, High), ED (0mL, 250mL, 500mL, and 750mL), and Alcohol x ED as fixed factors. [2] This line details the outcomes from the adjusted model for BrAC with Alcohol (Moderate, High), ED (0mL, 250mL, 500mL, and 750mL), Sex (Male, Female) and Alcohol x ED, Alcohol x Sex, ED x Sex, and Alcohol x ED x Sex as fixed factors, Subject as a random factor, and TLFB alcohol use frequency as a covariate. [3] This line details the outcomes for subjective intoxication change scores from the basic model with Alcohol (Placebo, Moderate, High), ED (0mL, 250mL, 500mL, and 750mL), and Alcohol x ED as fixed factors. The basic model was conducted with Maximum Likelihood Estimation and a diagonal covariance structure. [4] This line details the outcomes from the adjusted model for subjective intoxication change scores with Alcohol (Placebo, Moderate, High), ED (0mL, 250mL, 500mL, and 750mL), Sex (Male, Female) and Alcohol x ED, Alcohol x Sex, ED x Sex, and Alcohol x ED x Sex as fixed factors, Subject as a random factor, and TLFB alcohol use frequency as a covariate. All models were conducted with maximum Likelihood Estimation and a diagonal covariance structure. [b] These columns outline the main effects and interactions of the model. ED: energy drink; TLFB: Timeline Follow-Back past month alcohol use.

8.5.3.3 Beverage Rating Scale

The basic and adjusted models for perceived alcohol intake (4.8% a/v per drink unit) at 170 minutes showed a significant main effect of Alcohol; no other main effects or interactions reached statistical significance for either model (Table 2; Table 3). In the adjusted model, there was a large magnitude increase in reported alcohol intake in the high (*M*=2.0, *SD*=0.5) relative to the placebo (*M*=1.1, *SD*=0.5, *p*=.001, *g*=1.80) and moderate (*M*=1.5, *SD*=0.5, *p*=.114, *g*=1.00) alcohol groups, although this final comparison did not reach statistical significance. In turn, there was also a non-significant large magnitude increase in reported alcohol intake in the moderate relative to the placebo alcohol group (*p*=.349, *g*=0.80).

The basic and adjusted models for perceived ED intake (250mL with 80mg caffeine per unit) at 170 minutes showed significant main effects of Alcohol and ED; no other main effects or interactions reached significance (Table 2; Table 3). In the adjusted model, the placebo alcohol group (*M*=1.3, *SD*=0.4) had a large magnitude increase in perceived ED intake relative to the moderate (*M*=0.9, *SD*=0.4, *p*=.046, *g*=1.00), and high (*M*=1.0, *SD*=0.3, *p*=.233, *g*=0.85) alcohol groups; the difference in ED intake between the latter two conditions was of small magnitude (*p*=10.99, *g*=0.28). For the ED main effect, there was a moderate magnitude increase in reported ED intake after 500mL ED (*M*=1.5, *SD*=0.8) relative to 0mL (*M*=0.8, *SD*=0.7, *p*=.003, *g*=0.73), 250mL (*M*=0.9, *SD*=0.5, *p*=.002, *g*=0.60) and 750mL (*M*=1.0, *SD*=0.5, *p*=.042, *g*=0.55) ED; the final comparison did not reach significance. The reported intake after 0mL, 250mL, and 750mL ED did not differ significantly (*p*s>.855, *g*=0.12 to 0.21).

Table 3

Perceived Alcohol and Energy Drink Intake at 170 Minutes for Each Alcohol Group According to the Volume of ED Co-Ingested (Standard Error in Parentheses)

ED Condition	Alcohol Group		
	Placebo	***Moderate***	***High***
BRS Perceived Alcohol Intake[a]:			
0mL ED	1.3 (1.0)	1.7 (1.3)	2.4 (0.9)
250mL ED	1.3 (1.1)	1.4 (0.6)	1.9 (0.6)
500mL ED	1.2 (0.9)	1.4 (1.0)	2.0 (1.0)
750mL ED	1.2 (0.9)	1.4 (1.0)	2.0 (1.0)
BRS Perceived ED Intake[b]:			
0mL ED	1.1 (1.0)	0.7 (0.8)	0.7 (0.4)
250mL ED	0.8 (0.7)	0.8 (0.7)	0.9 (0.4)
500mL ED	1.6 (0.9)	1.1 (0.4)	1.5 (0.8)
750mL ED	1.2 (0.7)	1.0 (0.5)	1.0 (0.5)

[a] Perceived alcohol intake was reported on the Beverage Rating Scale (BRS) at 170 minutes; the intake scale ranged between 0 to 10 alcoholic drinks (4.8% a/v), increasing in 0.5 increments. [b] Perceived energy drink (ED) intake was reported on the Beverage Rating Scale (BRS) at 170 minutes; the intake scale ranged between 0 to 3 standard 250mL EDs (80mg caffeine each), increasing in 0.5 increments.

8.6 Discussion

Large magnitude decreases in peak objective intoxication were evident at 30 minutes after AmED relative to alcohol administration. This effect appeared dose-dependent; larger magnitude decrements in BrAC were evident with an increasing ED dose, with the lowest BrAC recorded after co-ingestion of an ED dose which exceeded Australian recommended maximum daily intake guidelines (i.e., 750mL). Similar results were evident on the descending limb (170 minutes post-administration), except that decrements in BrAC were similar after co-ingestion of an ED dose which matched or exceeded recommended maximum daily intake guidelines (i.e., 500mL or 750mL ED; Food Standards Australia and New Zealand, 2009). These results

support the premise that the sugar-sweetened ED beverage may be treated similar to a food, resulting in slower gastric emptying and alcohol absorption. While this effect has not been apparent in the literature to date (Marczinski et al., 2011; Marczinski et al., 2012, 2013; Peacock et al., 2013c), this may have been obscured by the low ED dose administered (Marczinski et al., 2011; Marczinski et al., 2012, 2013) or the use of a naturally-sweetened placebo beverage (Alford et al., 2012; Peacock et al., 2013c). Similar to previous research comparing natural and artificial sweeteners (Marczinski & Stamates, 2013), the decrement in BrAC evident after ingesting a naturally-sweetened mixer was evident at peak and on the descending limb, suggesting that the ED did not delay the time to peak BrAC but instead reduced the level of intoxication across the curve. Assessment of BrAC at regular intervals on ascending and descending limbs, as well as direct assessment of gastric emptying via ultrasound techniques, would further clarify these interpretations.

Previous survey research has shown that consumers self-report lower odds of sedation-based physiological and psychological side-effects and risk-taking in AmED versus alcohol sessions (Peacock et al., 2012), while typically ingesting on average 2.4 standard 250mL EDs in AmED sessions, a quantity demonstrated in the present study to cause large magnitude decreases in BrAC relative to alcohol alone [20]. However, decreased intoxication after AmED does not necessarily lead to reduced harms. Whilst not reaching traditional statistical significance, a moderate magnitude decrease in perceived intoxication was evident after administering the moderate

[20] It should be noted that the alcohol dose administered in the present study (moderate alcohol group: approximately 3.5 standard alcoholic drinks per 70kg male; high alcohol group: approximately 4.5 standard alcoholic drinks per 70kg male) is less than that retrospectively self-reported as typical alcohol intake in AmED drinking sessions (7.1 standard alcoholic drinks) by a convenience sample of Australian AmED consumers (*Chapter 3*).

alcohol dose with 750mL ED relative to without ED, even after controlling for differences in BrAC. Furthermore, these analyses showed that this effect was dependent on the volume of ED co-ingestion: moderate-to-large magnitude decreases in intoxication ratings were evident when the 750mL ED was co-ingested relative to 500mL and 250mL ED, with a large magnitude decrease in intoxication ratings after 500mL relative to 250mL ED. These results suggest that ED-induced reduced perception of intoxication may be specific to higher intake. ED-related changes in perceived intoxication were not apparent on the descending limb, indicating that these effects may be specific to peak intoxication. Furthermore, there was no evidence of ED-induced changes in perceived intoxication in the high alcohol group. Thus, it may be that the higher level of overall intoxication nullified the effect of ED on perception of intoxication: at both time points, the high alcohol group recorded higher intoxication ratings than the moderate alcohol group.

The moderate alcohol BrAC at which AmED-induced reduced perception of intoxication was observed reflects the BrAC limit for driving in Australia and the majority of the European Union. There is a strong body of research showing that alcohol consumers are poor at estimating their BrAC (Kloeden, Moore, & McLean, 1994; Wicki, Gache, & Rutschmann, 2000), even after estimation training (Aston & Liguori, 2013). Previous research has shown that AmED consumers typically report greater predisposition towards risk-taking relative to non-alcohol consumers (Brache & Stockwell, 2011). AmED-induced reduced perception of intoxication after excess ED intake, coupled with AmED consumers typically higher trait impulsivity (Brache & Stockwell, 2011), presents a high-risk profile for impaired decision-making and potentially increased engagement in risk-taking, such as driving under the influence

of alcohol. Only one study has been conducted to date directly assessing risk-taking following single low dose administration of AmED versus alcohol (Peacock et al., 2013c); assessment of dose-dependent changes in risk-taking behaviour post-AmED and alcohol administration could clarify whether these changes in intoxication translate into tangible increased harms for consumers.

There are a number of caveats in regards to these outcomes. The interpretation of the causes of these objective and subjective intoxication outcomes is based on comparison of AmED versus alcohol with artificially-sweetened mixers (i.e., diet beverages). AmED-induced decrements in BrAC and perceived intoxication relative to other naturally sweetened mixers has not been determined; other ED ingredients independently or interactively may cause additional decreases in BrAC relative to naturally-sweetened mixers with no other active ingredients. Clarification of the relative effects of these beverages is required to determine whether EDs offer equivalent or additional harms.

Furthermore, the environment in which consumption occurs must be considered. It has been well-established that estimates of alcohol impairment are less accurate in uncontrolled field settings relative to laboratory settings (Mills & Bisgrove, 1983); sensory distractions in the former setting are controlled in the latter setting. Thus, it may be that consumer' sensitivity to intoxication after co-ingesting three or two EDs relative to no ED may be altered in natural drinking environments. This is particularly relevant considering that consumers are typically aware of the beverages they are consuming. In contrast, the present study showed that, when blinded to beverage contents, participants could not meaningfully distinguish between receiving

no ED versus one or three EDs. While this outcome reinforces the success of the ED placebo manipulation, it does raise some questions as to consumers' sensitivity to the physiological and psychological outcomes of ED ingestion in general.

In regards to beverage blinding, participants in the moderate and high alcohol groups reported greater alcohol intake than in the placebo group, meaning that possible alcohol expectancy effects cannot be discounted. However, perceived alcohol intake did not differ according to whether participants had consumed AmED versus alcohol, suggesting that the present results should not be confounded by any potential expectancy effects. Given the presence of meaningful effect sizes for reductions in perceived intoxication but not traditional statistical significance, replication with larger samples or investigations with targeted design (e.g. subjective ratings of intoxication collected at consistent BrAC levels rather than through statistical adjustment) is also warranted to clarify the pharmacological effects of AmED relative to alcohol. Retrospective power analysis indicated that in order to detect within-subject perceived intoxication differences according to ED volume at each alcohol dose, a minimum of 16 participants would need to be run per group to reliably identify effects of this magnitude as significant (power=0.80, familywise α=.050).

In sum, AmED decreased objective level of intoxication relative to consuming alcohol alone, with greater decrements typically evident with increasing ED intake. Whilst generally not reaching statistical significance, moderate-to-large magnitude effects indicated that co-ingesting a moderate dose of alcohol with a high ED dose may result in lower intoxication ratings even after controlling for BrAC differences.

Replication of AmED-induced reduction in perceived intoxication in field settings and investigation of the behavioural consequences of AmED-alteration of objective and subjective intoxication is warranted.

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8.8 References

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Chapter 9: General Discussion

9.1 Introduction

Co-ingesting ED with alcohol is an increasingly popular consumption trend. The escalation in use has also seen an associated escalation in public concern regarding potential additional adverse effects (Australian Medical Association, December, 2012, January, 2013; United States Food and Drug Administration, November, 2010). The increase in public attention has been most dramatic over the duration of this doctoral research (2011-2013). Simultaneously, there has been an increase in research interest over this period; 63% (*n*=12) of the articles included in the systematic review (*Chapter 2*) were published between January, 2011 and May, 2013. The limited research available regarding the consumption patterns, antecedents, and consequences of use on commencement suggested that AmED use may be associated with a profile of increased alcohol-related harms. It was postulated that changes to the nature of intoxication (increased stimulation and decreased sedation) may alter consumers' perception of intoxication intensity, with negative physiological, psychological, and behavioural ramifications. Specifically, this altered intoxication state was thought to contribute to more risky alcohol consumption practices and potentially harmful motivations for use. However, there was no solid evidence base upon which to assess the validity of these claims due to a limited number of within-subject studies comparing outcomes of AmED versus alcohol consumption for the same individuals. As such, the primary aim of this thesis was to extend the preliminary body of literature and determine the consumption patterns, motivations for, and consequences of, AmED use. In response to mounting public concern, the latter was the predominant focus of this thesis, in particular the self-reported and objective behavioural outcomes of consumption.

In light of current endeavours towards AmED-related policy reform (Department of Health and Ageing, March, 2011), the research comprising this thesis is timely and relevant. Despite being completed at the end of the doctoral research, the systematic review included in *Chapter 2* was undertaken to provide a comprehensive summary of the current state of the literature, identifying the primary gaps in the evidence base regarding AmED harms. *Study 1* addressed a gap in the literature by examining the typical profile of AmED consumption amongst a community-based sample, as opposed to focusing on high-risk consumer groups, such as university students (*Chapter 3*). Analyses of physiological, psychological, and behavioural risk-taking outcomes in AmED versus alcohol drinking sessions self-reported by this sample were also conducted (*Chapter 4*). The resulting publication was the first in this field of research to circumvent systematic individual differences and adopt within-subject analyses (comparison of outcomes in AmED versus alcohol drinking sessions for the same individual) as opposed to between-subject analyses (comparison of outcomes for AmED versus alcohol consumers) to verify whether additional behavioural harms were self-reported for AmED use.

Study 2 was undertaken to determine whether within-subject retrospective self-reported outcomes were reflected in laboratory-based settings following acute dosing. This study addressed the lack of experimental research directly assessing the pharmacological effects of AmED. While the comparison of physiological and psychological outcomes of AmED versus alcohol was based on self-report (*Chapter 5*), objective measures of behavioural risk-taking and behavioural impulsivity were adopted to provide the first comprehensive objective assessment of these constructs in this field of research (*Chapter 6* and *7* respectively). The final study, *Study 3*, was

undertaken to assess the primary assumption underlying the theorised harms of AmED use: that AmED consumption reduces perceived intoxication relative to ingesting the same dose of alcohol without ED, despite equivalent objective intoxication (*Chapter 8*).

The primary findings from these studies (outlined in Table 1) will be summarised and integrated below to evaluate the evidence base for additional alcohol-related harms with AmED consumption.

9.2 Consumption Patterns and Motivations (*Research Question 1 and 2*)

The publication derived from *Study 1* (*Chapter 3*) was written with the aim of clarifying the consumption patterns and motivations for AmED use in the Australian community. In this study, Australian residents aged between 18 and 35 years completed an online survey regarding their recent simultaneous (i.e., two constituents mixed within the same beverage) AmED use. Analyses revealed that these consumers reported excess alcohol and ED intake in AmED sessions, despite mixing the two substances relatively infrequently. Notably, one-third of AmED consumers reported typically ingesting EDs in excess of recommended maximum daily intake guidelines (three or more standard 250mL EDs; approximately 240mg caffeine) (Food Standards Australia and New Zealand, 2009), with some consumers reportedly co-ingesting 10 standard 250mL EDs (approximately 800mg caffeine) with alcohol in one drinking session.

Table 1

Summary of the Major Thesis Findings

Study and Research Question	Chapter	Findings	Conclusion
Study 1, Question 1: What are the consumption patterns associated with AmED use at the community-level in regards to: (i) the frequency and quantity of intake, (ii) drink preferences, and (iii) consumption context?	3	AmED sessions were relatively infrequent compared to alcohol sessions. Alcohol and ED intake in AmED sessions significantly exceeded recommended intake guidelines. Participants generally used AmED whilst engaging in heavy drinking in public venues late at night.	Consumers may be using AmED in a setting and at a quantity which increases the likelihood of harmful alcohol outcomes.
Study 1, Question 2: What are the primary motivations driving AmED beverage choice at the community-level?	3	The primary motives for use related to the situational context, functional and hedonistic outcomes, and pleasurable taste. A small proportion of participants endorsed intoxication enhancement-related motives (e.g., increase alcohol intake, mask intoxication, hide alcohol's flavour).	Endorsement of intoxication enhancement-related motives was not wide-spread throughout this sample.
Study 1, Question 3: Are there any appreciable differences in the physiological, psychological, and behavioural outcomes of AmED versus alcohol consumption when comparing retrospective self-reported drinking experiences for the same individual?	4	Higher odds of self-reported stimulation-based physiological and psychological outcomes, and lower odds of sedation-based outcomes, were evident for AmED versus alcohol sessions. The odds of retrospective self-reported engagement in 26 risk-taking behaviours were significantly lower for AmED relative to alcohol sessions.	AmED may exert a dual-effect, increasing stimulation whilst decreasing sedation. Hypothesised increases in risk-taking post-AmED consumption were contradicted, with lower odds of risk-taking after AmED relative to alcohol.
Study 2, Question 4: Are any changes in self-reported physiological and psychological side-effects evident when comparing the effects of an acute dose of AmED and alcohol in a controlled environment for the same individual?	5	No interactive effects of AmED were evident for self-reported psychological outcomes. There were generally no interactive effects of AmED for self-reported physiological outcomes. Participants reported decreased heart palpitation ratings following AmED (peak mean BrAC .067%; approximately one standard 250mL ED) relative to the same dose of alcohol without ED.	Subjective state was typically altered due to the independent effects of alcohol or ED, rather than being modified by their interaction.

Table 1 Continued

Study and Research Question	Chapter	Findings	Conclusion
Study 2, Question 5.1: Are any changes in objectively assessed risk-taking evident when comparing the effects of an acute dose of AmED and alcohol in a controlled environment for the same individual?	6	There was no interactive effect of AmED on this behavioural outcome, although there was a significant, small magnitude increase in risk-taking after active ED (approximately one standard 250mL ED) relative to placebo ED. Ratings of intoxication did not differ following AmED versus alcohol administration; stimulation ratings were significantly higher in the former condition.	Risk-taking was only increased by ED intake, although the magnitude of effect indicated limited meaningful change. The absence of alcohol-induced increased risk-taking indicates that the task may have had reduced sensitivity to detect interactive AmED effects.
Study 2, Question 5.2: Are any changes in objectively assessed impulsive behaviour (specifically impulsive response initiation, response disinhibition, and impulsive decision-making) evident when comparing the effects of an acute dose of AmED and alcohol in a controlled environment for the same individual?	7	ED co-ingestion (peak mean BrAC .067%; approximately one standard 250mL ED) reduced alcohol-induced increases in impulsive response initiation for female participants when task difficulty was high. There were generally no treatment effects for response disinhibition and impulsive decision-making.	Interactive effects of AmED may be dependent on the behavioural impulsivity measure and differ by sex.
Study 3, Question 6.1: Are any changes in objective intoxication (i.e., BrAC) and subjective intoxication (i.e., ratings of perceived intoxication) evident when comparing the effects of alcohol alone and in combination with a high acute dose of ED (i.e., two or more standard 250mL EDs) in a controlled environment for the same individual?	8	BrAC was generally lower after consuming a moderate (peak mean BrAC ~ .050%) or high (peak mean BrAC ~ .065%) alcohol dose with ED (500mL or 750mL) relative to without ED at 30 and 170 minutes. Lower intoxication ratings were evident 30 minutes after co-ingesting a moderate alcohol dose with ED (750mL) relative to without ED, even after controlling for BrAC differences; no differences were evident following a high alcohol dose or at 170 minutes.	AmED decreased objective intoxication relative to alcohol consumed with artificially-sweetened mixer. AmED may cause reduced perception of intoxication after administration of moderate alcohol doses (BrAC ~.050%), even after accounting for BrAC differences.
Study 2, Question 6.2: Do objective and subjective intoxication outcomes differ dose-dependently according to the volume of ED co-administered with alcohol?	8	BrAC typically dose-dependently decreased with increasing ED intake, particularly after a moderate alcohol dose (BrAC ~.050%). Decreased intoxication ratings for the moderate alcohol group were only evident at the high ED dose (750mL) relative to the moderate (500mL) and low (250mL) ED dose; no dose-dependent effects were evident for the high alcohol group	Greater AmED-induced decreases in objective intoxication were evident with a higher ED dose. Reduced perception of intoxication following moderate alcohol consumption may be dose-dependent based on ED volume.

Further analyses undertaken for the publication in *Chapter 4* showed that AmED consumers typically exceeded Australian recommended maximum alcohol intake guidelines (National Health and Medical Research Council, 2009) in AmED and alcohol drinking sessions. However, average typical alcohol intake was significantly higher in the former session type. This excess intake is particularly concerning when noting that: (i) the majority of consumers ingested AmED in public licensed venues, (ii) nearly two-thirds of the sample consumed AmED during heavy drinking sessions, and (iii) over half of the sample typically began to consume AmED late at night (i.e., 9pm-12am).

Overall, the combination of excess intake and risky drinking context indicates that AmED consumers may be positioned for harmful outcomes post-consumption. However, analysis of motivations for use indicated that only a small percentage of consumers were using AmED with the intention of maximising alcohol intake (e.g., 'so I could drink more', 'to hide the flavour of alcohol'), despite general assumptions that AmED reduces perceived intoxication based on the oppositional effects of the two constituents (Ferreira et al., 2006). Approximately one-fifth of participants reported using AmED to stay out later; it was not clear whether consumers sought to maximise time socialising, maximise time drinking, or a combination of the two. In *Chapter 3* it was suggested that endorsement of intoxication enhancement-related motives may be specific to a subgroup of consumers. Future research breaking down the consumer group according to patterns of motivation endorsement could indicate whether there are AmED consumer subgroups differentially motivated in beverage choice and, if so, whether these groups differ in regards to: (i) demographics, (ii) trait personality, (iii) alcohol and ED intake in AmED sessions, and (iii)

consequences of AmED use, and alcohol use in general. This information would be most pertinent for public health awareness and psychoeducation regarding AmED harms, in that these approaches could be tailored to those consumers at the greatest risk of adverse outcomes.

The excess ED intake reported in *Study 1* is particularly concerning considering the unknowns surrounding this use. Food Standards Australia and New Zealand (2011) recommend that adults do not exceed 210mg caffeine per day to avoid negative side-effects. In *Study 1*, beverages categorised as an ED were clearly delineated and a standardised ED unit (standard 250mL ED containing 80mg caffeine) was provided for intake estimates[21]. This level of precision meant that typical intake estimates for specific ED ingredients could be calculated. However, total caffeine intake during AmED sessions may be elevated by use of other caffeinated alcohol mixers, such as cola soft drink (27.5mg caffeine per 250mL) (Food Standards Australia and New Zealand, 2010). Research assessing concomitant use of other substances with AmED could clarify the role of other stimulant-based products in adverse outcomes and indicate the need for consumer awareness campaigns to minimise AmED polydrug use.

It is also important to note that this study did not compare consumers' setting and motivations for use for AmED versus alcohol drinking sessions. The majority of motivations assessed were specific to co-ingesting (e.g., 'because I like the taste of alcohol and energy drinks together'). Comparison of general alcohol consumption

[21] This unit of measurement reflected typical ED composition in the Australian market; this exactness accounted for differences in volume packaging, where EDs can be purchased in shot (approximately 60mL), standard (approximately 250mL), and supersize (approximately 500mL).

motives (e.g., ‘to feel more comfortable’) could clarify whether AmED beverage choice is driven by different factors relative to alcoholic beverage choice in general, which is an important consideration if AmED is to be treated in a distinct manner to alcohol itself.

9.2.1 Future Directions

As noted above, the results from *Study 1* indicate that AmED consumers may be placing themselves in a situation of increased risk based on their AmED consumption patterns. However, there was little evidence of widespread harmful motives behind this beverage choice. There are several research questions which need to be addressed to determine whether AmED offers additional harms relative to alcohol in regards to the consumption patterns and motives for use:

1. Is the endorsement of potentially harmful motives for AmED use specific to a select group of consumers? If so, are these consumers at an increased risk of harm based on their demographic, personality, psychological, and behavioural profile?
2. Are consumers ingesting other caffeinated and stimulant-based products with AmED? Does concomitant use of other caffeinated products lead to excess caffeine consumption (i.e., exceeding recommended maximum daily intake guidelines)?
3. Do the consumption context and motivations for use differ for AmED versus alcohol use?

9.2.3 Implications and Summary

Overall, *Study 1* (*Chapter 3*) indicated that consumers are ingesting greater quantities of alcohol in AmED versus alcohol drinking sessions, enhancing the risk of negative outcomes by typically ingesting EDs in excess of Australian recommended maximum daily intake guidelines. Consumers may also be positioning themselves in a situation of increased risk in regards to the context for AmED use. However, the majority of consumers were not influenced in their AmED beverage choice by intoxication enhancement-related motives. While the reported consumption patterns indicate increased risk of adverse outcomes, it cannot be concluded that the relative risk is greater after AmED compared to alcohol, as consumption practices for AmED versus alcohol drinking sessions, and the extent of harms in each context, have not been compared.

9.3 Physiological and Psychological Outcomes (*Research Question 3 and 4*)

The aforementioned concerns regarding excess ED intake are further highlighted when examining the self-reported physiological and psychological outcomes of AmED consumption (*Chapter 4*, *5*, and *6*). *Study 1* (*Chapter 4*) showed that consumers self-reported increased odds of physiological and psychological outcomes linked to overstimulation (i.e., heart palpitations, sleep difficulties, agitation, tremors, jolt and crash episodes, increased speech speed, irritability, and tension) in AmED versus alcohol drinking sessions. These outcomes reflect those typically evident in cases of caffeine overconsumption (Reissig et al., 2009), and also mirror the adverse effects of recreational co-ingestion of ED with alcohol and/or other caffeine products reported to the New South Wales Poison Information Call Centre (Gunja & Brown, 2012).

This presentation profile is not unexpected in light of reported ED intake. In Australia, ED caffeine content is regulated and product packaging must display the caffeine content (mg per serving size/100mL), as well as an advisory statement for children, pregnant and lactating women, and individuals who are sensitive to caffeine (Food Standards Australia and New Zealand, 2009). Despite these requirements, one-third of Australian consumers who participated in *Study 1* reported typically ingesting EDs in excess of recommended maximum daily intake guidelines in AmED sessions (Section 9.2.1). No data was collected as to whether this excess consumption reflected an informed decision to exceed guidelines. These findings raise questions as to: (i) whether Australian consumers are aware of these guidelines, and (ii) whether similar ED intake and physiological and psychological outcomes are evident for consumers in those countries which have less stringent caffeine regulation or labelling requirements (Arria et al., 2013; Kole & Barnhill, 2013; Sepkowitz, 2013). It is important to note though that the present study may have underestimated rates of physiological and psychological side-effects. Outcomes were only identified as present in the last six months if participants responded 'half the time' or more often, excluding lower frequency occurrences (Rossheim et al., 2013), although subsequent analyses controlling for frequency of use has showed similar outcomes (Peacock et al., 2013b)

Study 1 also showed that the effects of AmED may not be restricted to stimulation-based outcomes; the odds of sedation-based outcomes, such as fatigue, nausea, slurred speech, and impairment of walking and vision, were lower for AmED versus alcohol sessions. As noted in Section 9.2, participants reported typically consuming more alcohol (approximately half a standard alcoholic drink) in AmED relative to

alcohol drinking sessions. Thus, the experience of decreased sedation outcomes is unlikely to simply reflect lower alcohol intake in AmED sessions. The change in the nature of intoxication is not necessarily advantageous for consumers; reducing physiological and psychological sedation cues which signal impairment may impact on the drinking experience, particularly behavioural decision-making (Marczinski et al., 2012).

Overall, the self-report data collected in *Study 1* suggests a dual effect of AmED use, with increased risk of stimulation outcomes and decreased likelihood of some sedation outcomes. This data did not indicate the clinical severity of side-effects, nor the dose at which these effects become evident. *Study 2* (*Chapter 5*) was partly undertaken to address the latter issue. In this study, self-reported physiological and psychological outcomes of AmED versus alcohol were compared following acute dosing in a single-blind, placebo-controlled, laboratory-based setting. This design allowed changes in subjective physiological and psychological state to be pharmacologically tied to the dose administered.

The results of *Study 2*, in part, contradicted those of *Study 1*. Despite assessing the same physiological constructs as in *Study 1*, there were generally no interactive effects of AmED on physiological outcomes in *Study 2*. The exception comprised decreased heart palpitation ratings following acute AmED relative to alcohol dosing, a finding contrary to the retrospective self-reported increased odds of heart palpitations reported for AmED relative to alcohol sessions in *Study 1*. *Study 2* also showed that there were no interactive effects of co-ingesting alcohol with ED for psychological outcomes assessed using the Profile of Mood States (POMS; McNair

et al., 1979). In contrast, direct assessment of stimulation and sedation via the Biphasic Alcohol Effects Scale (BAES; Martin et al., 1993) in *Study 2* (*Chapter 6*) showed increased ratings for the former state after AmED relative to alcohol, with no statistically significant difference in sedation ratings. This was somewhat surprising, considering that latent factor analyses using the POMS (short version) have shown that BAES Stimulation and POMS Vigour typically load on the same factor when characterising the subjective effects of alcohol (Ray, 2009)[22].

Thus, a contrary picture is presented: self-report of real-life drinking experiences indicates increased stimulation and decreased sedation after AmED relative to alcohol, whilst self-report following acute dosing in laboratory-based settings shows more mixed results, with little evidence of interactive effects. There are several possible explanations for this discrepancy in outcomes, including: (i) dose-dependent effects, (ii) expectancy effects, and (iii) the consumption context.

9.3.1 Dose-Dependent Effects

In *Study 1* (*Chapter 4*), consumers retrospectively self-reported typically ingesting 2.4 standard 250mL EDs with approximately 7.1 standard alcoholic drinks. In Study 2 (*Chapter 5*), approximately one standard ED (per 70kg person) and 3.5 standard alcoholic drinks were administered per participant. The general lack of statistically significant change in physiological and psychological state evident in *Study 2* could be a function of the low dose administered relative to that typically ingested in AmED drinking sessions. Only one experimental study has been conducted to date

[22] Note that BAES Sedation and POMS Depression/POMS Tension load on separate factors; 'Sedation' and 'Alleviation of Tension/Negative Mood' respectively.

assessing the psychological effects of higher ED intake using a multi-dose design (Alford et al., 2012). This study contrasted with the self-report findings of *Study 1*, in that there was some evidence that ED co-ingestion increased drowsiness and mental fatigue. However, the total volume of ED administered in the study by Alford et al. (2012) still fell below the typical intake retrospectively self-reported by Australian AmED consumers in *Study 1* (2 standard 250mL EDs versus 2.4 standard 250mL EDs). Furthermore, the authors acknowledge that between-subject differences in ratings may have contributed to the outcomes. No within-subject dose-dependent studies have been conducted to date.

Overall, these results could be tentatively interpreted to indicate that AmED physiological and psychological effects may be dose-dependent, with detectable differences of increasing magnitude evident at doses similar to, and higher than, than the average intake reportedly ingested in real-life settings. However, the paucity of within-subject research assessing the dose-dependent effects of bolus AmED and alcohol administration precludes any firm conclusions. Such research is necessary to provide an evidence base regarding the safety of current recommended intake guidelines.

9.3.2 Expectancy Effects

Previous research by Woolsey et al. (2010) has shown that AmED consumers have specific expectancies regarding the interactive effects of the two constituents. Specifically, surveyed United States university student athletes reported higher expectations of sleep difficulties, heart palpitations, and feeling nervous and jittery, and lower expectations of feeling dizzy and clumsy, in AmED versus alcohol

drinking sessions. It has been well-established that alcohol expectancies can differ between consumers based on non-pharmacological factors (e.g., parental history of alcohol abuse, alcohol advertising exposure, peer influence) (Brown, Creamer, & Stetson, 1987). These AmED-specific expectancies are not surprising considering the wealth of media publications outlining the harmful effects of AmED (Australian Medical Association, December, 2012, January, 2013; United States Food and Drug Administration, November, 2010). AmED-specific expectancy effects were controlled in *Study 2* (*Chapter 5*) by blinding participants to beverage content, with ED placebo manipulation shown to be effective. In contrast, *Study 1* (*Chapter 4*) involved retrospective self-report of physiological and psychological outcomes when participants had chosen, and were explicitly aware of, AmED beverage choice. Thus, it may be that expectancies specific to AmED impacted on self-reported outcomes: (a) during the drinking experience itself (within-session expectancy effect), and (ii) in the retrospective recall of the drinking experience (recall expectancy effect).

It is well-established that autobiographical memory is susceptible to error and bias; events are often reconstructed and recalled based on heuristic strategies (Bradburn, Rips, & Shevell, 1987), meaning they can be prone to distortion by events or information which arise before or after the event itself. Subjective states are particularly susceptible to bias and error. For example, participants who have quit smoking underestimate their number of lapses, and overestimate their negative mood during lapses, when comparing recalled outcomes with field recordings (Shiffman et al., 1997). Events which are deemed more salient (i.e., attract a greater amount of attention) are given greater causal attribution, regardless of the accuracy of these attributions (Fiske, Kenny, & Taylor, 1982). It is thought that people have a priori

expectations (cognitive schema) which determine the individual salience of events, meaning that evidence which is perceived as relevant (representative of causal attribution) is attended to and exaggerated, while information which is perceived as irrelevant is given less attention (Fiske et al., 1982). This theory could explain the outcomes of *Study 1*, in that AmED consumers may have specific cognitive schema regarding the interactive effects of these two constituents, and thus be more likely to attend to those subjective experiences which are seen as casually representative. AmED-specific schema could also retroactively interfere with recall, in that those events which fit with established ideas regarding AmED interactive effects are prominent, meaning that expectancy regarding AmED effects could influence recall of events.

Previous experimental research has shown that holding specific expectancies regarding the effects of alcohol combined with stimulants can influence performance independent of whether consumers actually co-ingest the stimulant (Fillmore et al., 2002; Heinz, de Wit, Lilje, & Kassel, 2013). While the results of *Study 1* could be explained by within-session expectancy effects, it is important to note that these effects were observed in past research when behavioural outcomes were measured objectively; ratings of subjective state in these previous studies were generally pharmacologically altered, regardless of expectancy manipulation. There has been no research conducted to date assessing the effect of AmED expectancy on physiological and psychological outcomes specifically, or behaviour in general, following acute dosing. Such research could determine the viability of consumer education strategies to facilitate accurate awareness of AmED side-effects. It should be noted though that the similarity between the physiological and psychological side-

effects reported in Study 1, and those reported in clinical data (Gunja & Brown, 2012), mitigate some of these concerns regarding the validity of outcomes.

9.3.3 Consumption Context

Another potential explanation for the discrepant physiological and psychological outcomes in *Study 1* and *2* are potential influencing factors in the consumption context, specifically: (i) concomitant use of other substances during AmED consumption, (ii) consumer sensitivity to caffeine and ED, and (iii) variation in drinking environment.

The outcomes of *Study 1* (*Chapter 4*) cannot be directly attributed to the pharmacological effects of AmED. Concomitant use of other caffeinated or stimulant-based products was not assessed in *Study 1*, meaning that consumers may have ingested other substances which, independently or in interaction with AmED, alter physiological and psychological state relative to when alcohol is consumed alone. Between-subject analyses show that AmED consumers are more likely to engage in illicit stimulant use than alcohol consumers after controlling for age and sex (Brache & Stockwell, 2011). Analyses of New South Wales Poison Information Call Centre data (Gunja & Brown, 2012) show that 71 out of 188 recreational exposures were related to co-ingestion of EDs with alcohol and/or other caffeinated products; the common side-effects reported by this subgroup mirror those reported in *Study 1*, including heart palpitations, tremors, and agitation. In contrast, ingestion of other substances was controlled in *Study 2* (*Chapter 5*). Participants were required to abstain from food for four hours, caffeine for eight hours, alcohol and medication for 24 hours, and illicit drugs for the duration of the study; participants regularly taking

prescribed medication (except the contraceptive pill) were excluded. Thus, the laboratory-based research provides a more reliable indication of the pharmacological effects of AmED alone relative to alcohol, although it should be noted that compliance was verbally ascertained (with the exception of alcohol abstinence, assessed via BrAC), rather than being confirmed via biological assays of drug levels.

Another advantage of the experimental research involved controlling for participants' sensitivity to the administered treatments. All participants in *Study 2* were regularly caffeine, ED, and alcohol consumers, with exclusion of those individuals reporting regular abuse of these substances. In contrast, there was no assessment of consumers' tolerance and vulnerability to caffeine in *Study 1*. Consumers who have rarely used ED or caffeine or have contraindicated medical conditions may be susceptible to overstimulation side-effects. This discrepancy in level of control in regards to consumer sensitivity may have contributed to the differing results of *Study 1* and *2*. To date, there is little information regarding AmED consumers' tolerance to caffeine, meaning that this consumer group's sensitivity to ED is difficult to determine.

Finally, the setting within which ratings were made in each study needs to be considered. In *Study 1*, participants reflected on their real-life drinking experiences. In contrast, in *Study 2* participants reported on their subjective state after double-blind, placebo-controlled dosing in an artificial environment. The same physiological constructs were assessed in both studies. However, the assessment environment for *Study 2* may not have been conducive to determining changes in these outcomes relative to baseline. For example, participants were asked to rate their walking ability

whilst being predominantly confined to a seated position. Alternatively, participants in *Study 1* may have been unable to recall information about all aspects of functioning across drinking sessions. To date, there has been no assessment of AmED physiological and psychological outcomes following acute intake in an uncontrolled field setting; this lack of research limits conclusions regarding the impact of the artificial assessment environment. Such research would circumvent issues of retrospective recall in an uncontrolled environment, increase ecological validity relative to assessment in a laboratory environment, and allow physiological and psychological changes to be linked to specific intoxication levels and ED intake.

9.3.4 Future Directions

As noted above, the discrepancy between self-report real-life and experimental outcomes raises several queries regarding the interactive effects of AmED, and highlights the primary methodological issues in identifying the pharmacological effects of co-ingestion. In order to determine whether any of the above factors contributed to the outcomes, the following research questions need to be answered:

1. Are self-reported physiological and psychological effects of AmED relative to alcohol dose-dependent when assessed within-subject? If so, what is the alcohol and/or ED intake threshold at which these relative changes in subjective state are consciously detected? Does the severity of side-effects increase with an increasing alcohol dose? Are these AmED-induced changes sufficient to warrant concern regarding their clinical severity?
2. Are self-reported AmED physiological and psychological outcomes a reflection of: (i) consumers' expectations of AmED effects, (ii) the pharmacological effect of AmED, or: (iii) a combination of the two?

3. Are self-reported AmED physiological and psychological outcomes a reflection of the pharmacological effect of AmED alone or a consequence of general overconsumption or elevated sensitivity to caffeine?
4. Are AmED consumers more vulnerable to physiological and psychological overstimulation following caffeine consumption relative to non-AmED consumers, or are adverse side-effects specific to a characteristically distinct subgroup?
5. Are self-reported physiological and psychological effects of AmED evident when assessed in an uncontrolled field setting following acute intake?

9.3.5 Implications and Summary

Overall, *Study 1* (*Chapter 4*) and *Study 2* (*Chapter 5* and *6*) indicated that consumers may be more likely to experience stimulation-based side-effects potentially related to caffeine overconsumption after ingesting AmED relative to alcohol. These effects were most prominent in consumers' retrospective self-report of drinking experience; despite biological plausibility, there was little indication in the experimental research that these findings may be pharmacologically-derived at the low doses administered. Retrospective self-report of drinking experiences also indicated that the likelihood of sedation-based side-effects may be decreased post-AmED consumption, although these findings were not evident in an experimental context.

9.4 Behavioural Outcomes (*Research Questions 3, 5.1 and 5.2*)

There has been a strong body of research published since the commencement of this doctoral research showing that AmED consumers report increased engagement in risk-taking relative to non-AmED consumers (*Chapter 2)* (e.g., L. Berger et al., 2013; Miller, 2012; Snipes & Benotsch, 2013). However, the dearth of research assessing rates of risk-taking in AmED versus alcohol drinking sessions for the same individuals has persisted. *Study 1* (*Chapter 4*) was partially undertaken to determine whether an Australian community-based sample of AmED consumers retrospectively self-reported greater rates of risk-taking in AmED versus alcohol sessions when reflecting on their drinking experiences in the last six months. Despite predictions that AmED would increase risk-taking relative to alcohol (based on the theory that AmED reduces perception of intoxication and consequently increases likelihood of risk-taking behaviour), it was shown that consumers consistently retrospectively self-reported lower rates of risk-taking in AmED versus alcohol drinking sessions. As noted in Section 9.3, participants reported significantly greater alcohol intake in AmED versus alcohol drinking sessions for the same time period (although the difference was half a standard drink), suggesting that differences in actual intake should not account for this discrepancy.

The results of *Study 2* align with the findings of de Haan et al. (2012), who showed that a Dutch university student sample were less likely to report risk-taking for AmED relative to alcohol sessions. However, the results contradicted expectations of AmED effects reported in the media (e.g., Australian Medical Association, December, 2012) and scientific academic publications (e.g., Pennay et al., 2011). The results of *Study 2* were validly critiqued by external researchers for potentially

underestimating rates of AmED rates of risk-taking on the basis of session frequency; lower frequency of AmED sessions relative to alcohol sessions meant that the opportunities for risk-taking were fewer in the former session (Rossheim et al., 2013). However, re-analysis of the data (Appendix D) showed that the original pattern of results held true even after matching AmED and alcohol session frequency.

Despite this, the retrospective self-report nature of the data still limits the interpretation of this data, particularly due to the sensitive nature of some items in requesting information about illicit behaviours. *Study 2* was undertaken to determine the effects of acute AmED versus alcohol dosing on an objective measure of risk-taking (*Chapter 6*), circumventing potential issues with self-report. This study revealed no interactive effect of AmED on performance. In contrast with *Study 1*, AmED administration resulted in a significant, yet small magnitude, increase in risk-taking relative to alcohol alone. However, this behaviour was driven by the ED component of the beverage, occurring regardless of whether alcohol was co-ingested. In fact, there was no statistically significant effect of alcohol administration on risk-taking (regardless of ED co-ingestion). These results are not wholly surprising given that the literature is mixed in regards to the effects of alcohol on objective measures of risk-taking (see Section 2.1.4), although reward-penalty contingencies were implemented in the present study to maximise sensitivity. However, the objective experimental risk-taking results of *Study 2* lack coherence with self-reported risk-taking outcomes in *Study 1*, and contradict popular conceptions regarding the adverse effects of AmED.

Examination of state-dependent changes in impulsive behaviour (*Study 2*, *Chapter 7*) lends further weight to these findings. Alongside increases in risk-taking, alcohol is thought to increase impulsive behaviour, although these effects are typically dependent upon the aspect of impulsive behaviour assessed (see Chapter 7). Measures of impulsive response initiation, response disinhibition, and impulsive decision-making were included in *Study 2* to determine whether AmED had a differential effect on impulsive behaviour relative to alcohol. Only impulsive response initiation registered AmED-induced changes in behaviour relative to alcohol alone, with *reductions* in impulsive behaviour evident for female (but not male) participants when task difficulty was elevated after AmED relative to alcohol administration. Similar to the risk-taking outcomes, there were generally no detectable treatment effects of alcohol or ED for response disinhibition and impulsive decision-making.

Thus, the results from this doctoral research are divergent: while retrospective self-report by consumers indicated *decreased* odds of risk-taking after AmED relative to alcohol, the experimental research showed that AmED may *increase* risk-taking, but only due to the ED component, and *decrease* aspects of impulsive behaviour, but only under specific conditions, relative to alcohol. Several explanations posed for these discrepant outcomes include: (i) task sensitivity, (ii) dose-dependent effects, (iii) limb-dependent effects, (iv) expectancy effects, and (v) impact of consumer characteristics.

9.4.1 Objective Task Sensitivity to Treatment Effects

A common factor across the objective measures of risk-taking and impulsive behaviour included in *Study 2* (*Chapter 6* and *7*) was the general lack of detectable alcohol treatment effects. As noted in *Chapter 6*, the chosen measure of risk-taking, the Balloon Analogue Risk Task (Lejuez et al., 2002), may have underestimated the rate of risky behaviour: the index of risk-taking did not take into account the number of balloon pumps on those trials when participants engaged in the maximum level of risk (i.e., pumped the balloon to the predetermined explosion point). These results, coupled with the general inconsistency in experimental research in showing alcohol-induced increases in risk-taking (Section 2.1.4), suggests that task sensitivity may be partially accountable for the discrepancy between *Study 1* and *2* outcomes, particularly considering the wealth of epidemiological data linking alcohol use and risk-taking. In Section 2.1.4, research conducted by Euser et al. (2011) was summarised, showing that assessing overall risk-taking outcomes may obscure changes in gambling strategy throughout the task. In this study, participants administered alcohol (mean peak BrAC .077%) decreased their rate of risk-taking throughout the task, whilst those administered placebo showed the converse. Analysis of the overall average number of pumps did not reveal these treatment outcomes. Thus, it may be that alcohol administration alters risky decision-making strategy, as opposed to overall rates of risk-taking behaviour, in experimental contexts[23]. Comparative analysis of BART trial blocks after adopting an automatic response paradigm to avoid excluding trials on which risk-taking was greatest could

[23] Breakdown analyses according to trial block were not implemented at the time of publishing the manuscript within *Chapter 6* due to concerns regarding statistical power, as the sample size was determined a priori based on sufficient power to detect a moderate magnitude effect for the interaction of alcohol and ED.

increase sensitivity to the effects of alcohol, administered independently and in combination with ED; increased statistical power relative to the present study will be required to detect these potential effects.

The only behavioural impulsivity task to register interactive AmED effects, the Immediate Memory/Delayed Memory Task (IMT/DMT; Dougherty et al., 2002), has demonstrated sensitivity to alcohol in several studies (Section 2.7.2). However, the explanation of poor task sensitivity does not fully account for the general lack of statistically significant treatment effects for the measure of response disinhibition, the Cued Go/No-Go task, and the measure of impulsive decision-making, the Experiential Discounting Task (EDT; Reynolds & Schiffbauer, 2004). In contrast with *Study 2*, Marczinski et al. (2012) showed that alcohol (mean peak BrAC .089%) increased the proportion of inhibition failures[24] relative to placebo; this effect was not diminished by co-administration of ED. Similarly, Reynolds et al. (2006b) showed that alcohol (mean peak BrAC ~.076%)[25] increased impulsive decision-making on the EDT relative to placebo.

It is important to note that there were some methodological concerns regarding the Cued Go/No-Go task and the EDT in the current study, primarily: (i) the time-window for categorisation of commission errors for the Cued Go/No-Go task, and (i) the percentage of EDT trials which had to be excluded due to a failure to reach

[24] Proportion of inhibition failures was defined as responses to valid cued no-go targets and invalid cued no-go targets

[25] Note that the approximate mean BrAC for Reynolds et al. (2006b) was extracted from Figure 1 of the publication.

indifference between the standard and delayed option. The reduced power as a consequence of these limitations may have decreased sensitivity to treatment effects.

9.4.2. Dose-Dependent Effects

As noted above, the Cued Go/No-Go task and the EDT (Reynolds & Schiffbauer, 2004) have registered alcohol-induced increases in impulsive behaviour in past research, despite a general absence of detectable alcohol treatment effects in *Study 2* (*Chapter 7*). This previous research (Marczinski et al., 2011; Reynolds et al., 2006b) involved administration of alcohol doses which exceeded those used in the present study (0.65g/kg and 0.80g/kg alcohol versus 0.50g/kg alcohol, respectively). The study by Reynolds et al. (2006b) showed that increases in impulsive decision-making on the EDT were only evident after ingesting 0.80g/kg alcohol; administration of 0.40g/kg alcohol (mean peak BrAC ~.037%) did not alter performance relative to placebo alcohol. Furthermore, in *Study 2* these tasks were administered later in the session (Cued Go/No-Go task: 75 minutes; EDT: 100 minutes after commencing beverage administration); mean BrAC at these time points (mean BrAC .055% and .046%) was considerably lower than the BrAC at the time of testing for these previous studies (Marczinski et al., 2011; Reynolds et al., 2006b).

This past research suggests that alcohol may dose-dependently increase objectively measured impulsive and risky behaviour. Dose-dependent increases in risk-taking are well-established in epidemiological data. For example, analysis of data from fatal driver injuries in single-vehicle crashes indicates that with each .02% increase in BrAC when intoxicated, there is a nearly two-fold increase in the risk of being in a

fatal accident (Zador, 1991). Co-ingestion of ED adds an additional level of complexity when considering potential dose-dependent effects. The dose of ED and alcohol administered in *Study 2* (approximately 1 standard 250mL ED and 3.5 standard alcoholic drinks) fell short of the typical intake reported by AmED consumers in *Study 1* (approximately 2.4 standard 250mL EDs and 7.1 standard drinks) for the same time period for which a decreased likelihood of risk-taking in AmED sessions was reported. While the results of *Study 1* cannot be solely attributed to the pharmacological effects of AmED, the outcomes could be interpreted to suggest that appreciable changes in risky and impulsive behaviour may be a consequence of greater alcohol and ED intake than that administered in *Study 2*. However, this conclusion remains tentative due to the absence of research replicating the current experimental findings, assessing the effects of higher alcohol and ED intake volume, or adopting more complex dosing protocols to determine the dose-dependent effects of AmED versus alcohol on risk-taking.

Field research assessing exiting bar patrons' intention to drive while intoxicated showed that AmED consumers were more likely to report prospective risk-taking relative to those who had consumed alcohol, even after controlling for differences in BrAC (Thombs et al., 2010). While the level of intoxication in the study by Thombs et al. (2010) (AmED consumer: mean BrAC .109%; alcohol consumer: mean BrAC .081%) was higher than that achieved in *Study 2* (AmED condition: mean peak BrAC .068%; alcohol condition: mean peak BrAC .067%), the quantity of ED co-ingested was not specified. Given the greater risk-taking propensity of AmED consumers, between-subject comparisons preclude causal attributions regarding AmED and risk-taking. Furthermore, BrAC and risk-taking was only assessed at the

conclusion of drinking. To date, there has been no research, field or laboratory-based, assessing risk-taking at varying levels of intoxication and after differing ED intake.

9.4.3. Breath Alcohol Concentration Limb-Dependent Effects

In addition to dose-dependency, another potential pharmacological explanation for the discrepant outcomes for *Study 1* and *2* could be limb-dependent effects. As noted in Section 9.4.2, objective measures of risk-taking and impulsive behaviour in *Study 2* (*Chapter 6* and *7*) were administered on the descending limb. It is well-established in the literature that alcohol consumers typically display acute tolerance over the blood alcohol concentration curve; that is, some aspects of alcohol-induced behavioural impairment are of lesser intensity when assessed at the same point on the descending limb (e.g., BrAC descending .050%) relative to the ascending limb (e.g., BrAC ascending .050%) (Schweizer & Vogel-Sprott, 2008; Vogel-Sprott, 1979). As the primary risk-taking behaviours assessed in *Study 1* (e.g., driving behaviour, sexual risk-taking) may occur after the cessation of drinking (Davis et al., 2009; Fillmore et al., 2008), the objective measures for *Study 2* were administered on the descending limb. However, there is mixed evidence as to whether acute tolerance is evident for risk-taking on objective measures. For example, Fillmore et al. (2005) found no evidence of acute tolerance to alcohol-induced impairment of response inhibition on a Cued Go/No-Go task (peak mean BrAC .083%). However, in contrast, Streufert et al. (1992) reported that participants tended to display a more risky choice strategy on a visuo-motor task after ingesting alcohol (peak mean BrAC .099%) relative to placebo when tested on the ascending limb; no alcohol treatment effects were detected on the descending limb.

If alcohol differentially affects risk-taking according to BrAC, the results of *Study 2* cannot be generalised to the whole intoxication experience; the interactive effect of co-ingesting ED with alcohol may differ according to the level of alcohol-induced impairment experienced on the ascending and descending limb. There is no research available to date assessing whether AmED similarly reduces, maintains, or attenuates, alcohol-induced changes in risk-taking across the curve. As noted in Section 9.4.2, field research by Thombs et al. (2010) has shown that exiting bar patrons under the influence of AmED are more likely to report risk-taking intentions (i.e., intention to drive a vehicle intoxicated) than those who are under the influence of alcohol. While BrAC at the time of reporting was measured in this study, the single encounter with participants exiting the bar meant that the limb of the curve could not be determined. A study adopting a similar design, but with multiple assessment time points, could characterise real-world fluctuations in risk-taking intention across ascending and descending limbs.

9.4.4. Expectancy Effects

While the above explanations have focused on pharmacological effects, the role of environmental factors should also be emphasised in explaining the discrepant outcomes between *Study 1* and *2*. It has been well-established that expectancy of consuming alcohol can influence risk-taking behaviour independent of pharmacological outcomes. McMillen and Wells-Parker (1987) found that participants who thought they had ingested a moderate alcohol dose displayed more risk-taking on a driving simulator task relative to those who thought they had received a high or no alcohol dose; actual administration of alcohol (45.lmL/18kg,

13.lmL/18kg[26]) did not appreciably alter outcomes. These results suggest that consumers' specific expectations regarding the effects of alcohol consumption can alter risk-taking, regardless of actual alcohol ingestion.

This premise is supported in subsequent research looking at expectancies regarding the interactive effects of alcohol and caffeine on performance. Participants led to expect attenuation of alcohol induced-psychomotor impairment following caffeine co-ingestion displayed greater impairment relative to those expecting equivalent outcomes after alcohol, regardless of whether alcohol (mean peak BrAC .079%) was consumed with caffeine (4.0mg/kg) (Fillmore et al., 2002). Although these results do not apply specifically to risk-taking, this body of research suggests behaviour may be modified by expectations of the effects of alcohol, consumed independently and in combination with other substances.

As noted in Section 9.3.2, consumers report specific expectancies regarding the physiological and psychological AmED outcomes. These expectancies also appear to encompass the behavioural consequences of co-ingestion. Woolsey et al. (2010) found that consumers expected to display more aggression, and be more likely to drive a vehicle while intoxicated, during AmED versus alcohol sessions. *Study 2* of this doctoral research controlled for expectancy effects by blinding participants to beverage content. However, in *Study 1* participants retrospectively reported on instances of informed beverage choice, where there may have been certain motives behind, and expectations for, AmED use, introducing the possibility of within-session expectancy effects and/or recall expectancy effects (see Section 9.3.2). There

[26] BrAC was not specified in the study by McMillen et al. (1989).

has been no experimental research conducted to date determining the relative influence of expectancy versus pharmacology on AmED-related risk-taking behaviour. As such, this premise regarding AmED expectancy effects remains tentative, particularly as AmED-related expectancies of greater risk-taking contradict the self-reported results of *Study 1* showing decreased odds of risk-taking after AmED.

9.4.4. Consumer Characteristics

The final potential explanation for the discrepant outcomes of *Study 1* and *2* centres on the trait characteristics of the consumer themselves. As noted in *Chapter 2*, recent research has demonstrated that AmED consumers are typically higher in risk-taking propensity and trait impulsivity relative to alcohol consumers. *Study 1* (*Chapter 4*) showed that behaviours which are illicit (e.g., driving a motor vehicle whilst intoxicated) or have severe immediate consequences (e.g., requiring emergency medical treatment) showed lower levels of endorsement relative to those behaviours which are legal with remote (e.g., smoked cigarettes) or less severe (e.g., spent more money than planned) consequences. Being beyond the scope of the present research, no latent class analyses were undertaken to determine whether endorsement of the former type of risk-taking behaviour was spread across the AmED sample or specific to a small subgroup of consumers with high trait impulsivity. However, it may be that the degree of AmED-induced state-dependent impulsive behaviour differs according to whether the consumer's trait impulsivity tendencies are low or high. As noted in *Chapter 7*, participants in *Study 2* reported lower trait impulsivity relative to normative levels. Thus, the results of *Study 2* may not be generalisable to the AmED consumer demographic as a whole. To date, there has been no research assessing

whether there is an interaction between trait and state-dependent impulsivity for AmED consumers post-consumption. Such research is pertinent, as it can clarify whether consumer education campaigns should be tailored to address this specific high-risk subgroup.

9.4.5. Future Directions

As reviewed above, there are several potential explanations for the discrepancy between retrospective self-reported and objective acute risk-taking behaviour evident in this research. These explanations are not necessarily discrete; it may be that a combination of methodological (e.g., task sensitivity), pharmacological (e.g., dose- and limb-dependent outcomes), psychological (e.g., AmED and alcohol expectancy effects), and dispositional (e.g., trait impulsivity) factors co-contribute. In order to determine the validity of the above explanations, the following research questions need to be answered:

1. Are differences in risk-taking after acute dosing of AmED relative to alcohol evident on objective laboratory-based measures of risk-taking when task sensitivity is maximised? If so, do these differences reflect those retrospectively self-reported by consumers?
2. Are differences on laboratory-based objective measures of impulsive response initiation, response disinhibition, and impulsive decision-making evident after acute dosing of AmED relative to alcohol when statistical power is increased?
3. Are the relative effects of AmED versus alcohol on objective measures of risky and impulsive behaviour dose-dependent for the range of alcohol

consumed in real-life drinking sessions? Are these effects evident in uncontrolled field settings?

4. Are the relative effects of AmED versus alcohol on objective measures of risky and impulsive behaviour dependent on whether performance is assessed during ascending, peak, or descending BrAC? Are these effects evident in uncontrolled field settings?
5. Are self-reported and objective risk-taking outcomes evident after ingesting AmED relative to alcohol a consequence of pharmacology, differential expectancies of beverage outcomes, or a combination of these factors?
6. Are AmED consumers higher in trait impulsivity more or less likely to engage in risky and impulsive behaviour after consuming AmED relative to those consumers lower in trait impulsivity? If yes, are there differential effects of AmED relative to alcohol on risky and impulsive behaviour for high and low trait impulsivity AmED consumers?

9.4.5. Implications and Summary

This doctoral research was partially undertaken to address the lack of research assessing whether AmED poses additional behavioural harms relative to alcohol alone. Despite a proliferation in AmED research, the paucity of evidence specific to risky and impulsive behaviour has persisted. This scarcity of research makes reconciliation of the present results even more challenging, particularly considering that the outcomes contradict popular assumptions that AmED ingestion offers additional harms by increasing the likelihood of risky and impulsive behaviour relative to alcohol alone. Retrospective self-report by Australian AmED consumers in *Study 1* (*Chapter 5*) showed consistently decreased odds of risk-taking behaviour

in AmED versus alcohol drinking sessions. In contrast, administration of an objective measure of risk-taking following acute dosing in *Study 2* (*Chapter 6*) showed a significant increase in risk-taking after AmED relative to alcohol. However, this effect was driven purely by the ED component, with increases in risk-taking evident regardless of whether alcohol was consumed. Furthermore, the increase in risk-taking was of such small magnitude as to have limited practical relevance for consumers in the night-time economy. Similarly, *Study 2* (*Chapter 7*) showed that AmED and alcohol administration typically did not alter objectively measured impulsive behaviour, with only one measure of impulsive behaviour detecting decreases in alcohol-induced impairment post-AmED consumption, and only under certain task conditions (high task difficulty) and in certain demographic groups (female participants).

Overall, these results could be interpreted to suggest that AmED does not appreciably alter impulsive or risky behaviour in a manner which increases the likelihood of harm, and may even reduce the probability of hazardous behavioural outcomes. However, it is more likely that the link between AmED consumption and risk-taking is not straightforward; whether AmED increases, maintains, or attenuates alcohol-induced changes in risk-taking may be dependent on pharmacological (e.g., ED and alcohol dose), psychological (e.g., expectancy effects), dispositional (e.g., trait impulsivity), and methodological (e.g., task sensitivity) factors. The shortage of research on this topic precludes any definitive conclusions regarding the potential mediating role of these factors.

9.5 Objective and Subjective Intoxication Outcomes (*Research Questions 6.1 and 6.2*)

As noted in Section 9.4.1, the research assessing the behavioural consequences of AmED use was based on the assumption that AmED consumption creates a state of 'wide-awake drunkenness' (Arria & O'Brien, 2011), whereby the stimulatory nature of the ED masks the depressant effects of alcohol which act as a subjective indicator of intoxication. As a consequence of this, it was theorised that AmED consumers may self-report lower intoxication relative to when consuming an equivalent quantity of alcohol without ED, impairing decision-making and increasing the likelihood of risk-taking behaviour.

Study 1 (*Chapter 4*) was consistent with this premise of AmED-induced increased stimulation and decreased sedation, with consumers' retrospectively self-reporting greater odds of physiological and psychological stimulation-based outcomes, and lower odds of sedation-based outcomes, in AmED relative to alcohol drinking sessions. While assessment of physiological and psychological outcomes in an experimental content (*Study 2, Chapter 5*) did not show the same pattern of results, direct assessment of these constructs in this same study (*Chapter 6*) showed AmED-induced elevation of perceived stimulation. However, in contrast with predictions, ratings of perceived intoxication did not differ in *Study 2* (*Chapter 6*) according to administration of AmED versus alcohol. This pattern of equivalent perceived intoxication coupled with increased stimulation has been observed in the alcohol and caffeine (Attwood et al., 2012), and alcohol and ED (Marczinski et al., 2012) experimental literature. In fact, equivalent ratings of perceived intoxication after AmED and alcohol have been consistently shown across the few experimental

AmED studies conducted to date (Marczinski et al., 2011; Marczinski et al., 2012, 2013).

Based on this research, and the evidence presented within this thesis (*Chapter 4*, *5*, and *6*), it has been theorised by Attwood et al. (2012) and the present author (*Chapter 6*) that AmED changes the nature (i.e., perceived stimulation and sedation), as opposed to the intensity, of intoxication. The conclusion calls into question the causal link between AmED use and increased risk-taking (Section 9.4), as the alteration in perceived intensity of intoxication was the presumed mechanism underlying this effect. This hypothesis was based on a strong body of research showing that alcohol heightens intention to engage in risk-taking behaviour via changes in perceived intoxication (e.g., Davis et al., 2009).

However, it was noted that there was no research assessing the dose-dependent effects of bolus AmED versus alcohol intake on perceived and objective intoxication. As noted in Section 9.3.1 and 9.4.2, the previous experimental research (including *Study 2* of this thesis) was limited to administering a single low ED dose in combination with a single alcohol dose (Marczinski et al., 2011; Marczinski et al., 2012, 2013), despite consumers reportedly typically ingesting EDs in excess of recommended maximum daily intake guidelines (*Study 1*, *Chapter 4*). The only study to investigate the effects of a higher ED dose (i.e., two standard 250mL EDs) did not directly assess perceived intoxication (Alford et al., 2012) and administered a placebo with an unspecified quantity of natural sugars. Ingestion of alcohol with a naturally-sweetened mixer has been shown to cause significantly lower BrAC relative to an artificially-sweetened mixer, despite equivalent ratings of perceived

intoxication (Marczinski & Stamates, 2013). The results of this past research suggested that naturally-sweetened mixers, such as ED, may alter the degree of objective intoxication, with implications for consumers' perceived level of intoxication; whether this effect is dose-dependent (greater volume of naturally-sweetened mixer equals greater decrements in intoxication) was not examined.

Consequently, the aim of *Study 3* (*Chapter 8*) was to address the lack of research assessing the dose-dependent effects of AmED relative to alcohol on objective and subjective intoxication. Two alcohol doses (moderate dose: target BrAC .050%; high dose: target BrAC .080%) were co-administered with: (i) an artificially sweetened placebo ED, (ii) 250mL ED, an equivalent dose to that administered in *Study 2* and in past research (Ferreira et al., 2006; Marczinski et al., 2011; Marczinski et al., 2012), (iii) 500mL ED, an equivalent dose to the Australian recommended maximum daily intake guidelines (Food Standards Australia and New Zealand, 2009), and (iv) 750mL ED, a similar dose to that typically ingested by consumers in AmED sessions (*Study 1*, *Chapter 3*).

9.5.1 Objective Intoxication

For *Study 3 (Chapter 8),* analyses showed moderate-to-large magnitude decreases in objective intoxication at peak (30 minutes) after AmED relative to alcohol; this effect was linear, with larger decrements in BrAC evident with an increasing ED dose. A similar pattern was observed on the descending limb (170 minutes), except that the greatest decrement in BrAC was observed after 500mL ED for the high alcohol dose condition. These results suggest that co-ingestion of ED may decrease actual levels of intoxication, with increasing ED volume linked to decreased BrAC.

The consistency of the dose-dependent effect at peak BrAC and on the descending limb suggests that it is likely that ED did not delay the time to peak BrAC but instead reduced intoxication across the BrAC curve.

Based on previous research (Marczinski & Stamates, 2013; Rossheim & Thombs, 2011; Wu et al., 2006), it is theorised that the naturally-sweetened beverage is treated similar to a food, resulting in slower gastric emptying and alcohol absorption (*Chapter 8*), although it is important to note that rate of gastric emptying was not directly measured in *Study 3*. This explanation can be applied to the equivalent BrAC evident in *Study 2*. *Study 2* involved administration of a sugar-matched placebo, meaning that the carbohydrate content of active and placebo beverages did not differ. In contrast, in *Study 3* the active ED contained approximately 27g sugar per 250mL, as well as other active ingredients (e.g., 80mg caffeine, 1000mg taurine) as per the typical marketed beverage, while the placebo ED had no active ingredients (0g sugar, 0mg caffeine, 0mg taurine).

These results of *Study 3* also offer a potential explanation for the outcomes of *Study 1* (*Chapter 4*). In *Study 1*, consumers self-reported lower odds of sedation-based physiological and psychological side-effects and risk-taking behaviour in AmED versus alcohol sessions. They also reported ingesting on average 2.4 standard 250mL EDs in AmED sessions, a quantity shown in *Study 3* to cause large magnitude decreases in BrAC relative to alcohol without ED. The lower level of intoxication experienced as a consequence of this excess ED intake could impact on the experience of sedation side-effects, which are typically evident at higher BrAC (Addicott, Marsh-Richard, Mathias, & Dougherty, 2007; Earleywine & Erblich,

1996; Pohorecky, 1977). Furthermore, this lower BrAC could alter the degree of alcohol-induced impairment of decision-making and subsequent engagement in risk-taking, with evidence that some executive functions are impaired only at higher alcohol doses (Zoethout et al., 2011).

There are a number of caveats in regards to this explanation. In *Study 1*, consumers reported ingesting approximately half a standard drink more in AmED relative to alcohol drinking sessions; AmED-induced decrements in BrAC may have been offset by this additional intake. Furthermore, this interpretation is based on the premise that consumers in *Study 1* were ingesting alcohol with artificially-sweetened mixers in their alcohol drinking sessions. It may be that other ED ingredients (e.g., caffeine) independently or interactively cause additional decreases in BrAC relative to naturally-sweetened mixers with no other active ingredients. No comparison of BrAC levels after AmED relative to other naturally-sweetened mixers was undertaken in *Study 3*.

9.5.2 Subjective Intoxication

The primary outcome of interest from *Study 3* (*Chapter 8*) was the moderate-to-large magnitude decrease in perceived intoxication at peak BrAC after administration of a moderate alcohol dose with 750mL ED relative to alcohol without ED or with 250mL or 500mL ED, evident after controlling for differences in BrAC. These effects were not apparent for the high alcohol dose at peak BrAC, suggesting that the higher objective intoxication may have nullified the effect of ED on judgement of intoxication. AmED-induced reduced perception of intoxication was also not evident

after either alcohol dose on the descending limb, indicating that these effects may be larger in magnitude during the earlier portion of the BrAC curve.

The primary cause for concern is that the moderate alcohol BrAC at which AmED-induced reduced perception of intoxication was observed reflects the legal limit for driving in Australia and in the majority of the European Union. AmED-reduced perception of intoxication after excess ED intake, coupled AmED consumers' typically higher trait impulsivity, presents a high-risk profile for impaired decision-making and potentially increased risk-taking. There is a strong body of research showing that alcohol consumers are poor at estimating their BrAC (Kloeden et al., 1994; Wicki et al., 2000), even after estimation training (Aston & Liguori, 2013). Reduced perception of intoxication could cause consumers to believe their BrAC falls below the drink-driving limit, despite recording an objective BrAC which exceeds this limit. This conclusion remains tentative, as no assessment of perceived ability to drive was included in the present study.

However, the results of *Study 1* (*Chapter 5*) are somewhat contrary to this interpretation; consumers self-reported *lower* odds of risk-taking after ingesting AmED relative to alcohol, despite the typical ED intake for these consumers approximating the high ED dose which produced decrements in perceived intoxication in *Study 3*. However, the average self-reported alcohol intake for AmED sessions exceeds the high alcohol dose (approximately 4.5 standard alcoholic drinks per 70kg person) administered in *Study 3*, suggesting that the effect of ED on perceived intoxication may have dissipated due to higher BrAC. Furthermore, the differential effect of ED on perceived intoxication at peak BrAC versus the

descending limb may also contribute to the discrepant findings, in that the risk-taking behaviour reported in *Study 1* may have occurred at peak BrAC or on the ascending or descending limb of the curve; ratings were not consistently assessed across the BrAC curve in *Study 3*. Finally, the environment in which consumption occurs must be considered. In *Study 3*, participants were explicitly asked to reflect on their level of intoxication; sensory distractions which may be present in a natural drinking environment were controlled. It has been well-established that estimates of alcohol impairment are less accurate in uncontrolled field settings relative to the laboratory (Mills & Bisgrove, 1983). Thus, it may be that consumer sensitivity to intoxication after co-ingesting three EDs relative to two, one or no ED with alcohol may be altered in natural drinking environments.

In contrast, the findings of *Study 3* partially account for the perceived intoxication outcomes of *Study 2* (*Chapter 6* and *7*). While the moderate dose of alcohol ingested in both studies was matched (0.50g/kg), *Study 2* only involved administration of approximately one 250mL ED with alcohol. As evident from *Study 3*, co-ingestion of this low ED dose would not be sufficient to alter appreciably perceived intoxication relative to alcohol alone, with only a small magnitude decrease evident in *Study 3* for this comparison after controlling for BrAC. Unfortunately, perception of stimulation and sedation was not analysed for *Study 3*. This data could indicate whether the change in the intensity of intoxication after ingesting AmED with a high ED dose was coupled with a change in the nature of intoxication (i.e., increased stimulation).

However, it is the significant, yet small magnitude, increase in risk-taking in *Study 2* which is most interesting in light of the findings of *Study 3*. The absence of AmED-induced underestimation of intoxication should theoretically lead to equivalent rates of risk-taking after AmED and alcohol. Whether this magnitude of effect increases with underestimation of intoxication following co-ingestion of a high ED dose remains to be seen, as *Study 3* forms the first preliminary evidence to date regarding the dose-dependent effects of AmED on objective and subjective intoxication.

9.5.3 Future Research Directions

Several questions are raised as a consequence of this investigation into the dose-dependent effects of alcohol and ED. Suggested future areas of research revolve primarily around clarifying the mechanisms underlying AmED-induced decrements in BrAC and investigating the consequences of potential AmED-induced decreases in perceived intoxication. The primary questions which need to be addressed are:

1. Does objective measurement of gastric emptying rate via ultrasound indicate that an increasing ED dose is associated with a decreasing rate of absorption when co-ingested with alcohol?
2. Are ED-induced decrements in BrAC attributable only to the carbohydrate content or are other ED ingredients independently or interactively responsible for this decrease in objective intoxication?
3. Is the decrement in BrAC observed after ED equivalent to that observed after co-ingesting the same volume of other naturally sweetened mixers (e.g., caffeinated cola)?
4. Is AmED-induced reduced perception of intoxication after a high ED dose at peak BrAC associated with an overestimation of perceived ability to drive?

5. Is AmED-induced reduced perception of intoxication after a high ED dose at peak BrAC evident consistently across the BrAC curve?
6. Is AmED-induced reduced perception of intoxication after a high ED dose (relative to a moderate or low ED dose, or no ED) at peak BrAC evident in uncontrolled field settings at objectively matched BrAC levels?
7. Is the change in the intensity of perceived intoxication evident after co-ingesting a high ED dose at peak BrAC accompanied by a change in the perception of the nature of intoxication (i.e., perceived stimulation and sedation)?
8. Is AmED-induced reduced perception of intoxication after a high ED dose at peak BrAC associated with increased risk-taking on objective behavioural measures?

9.5.3 Implications and Summary

The results of *Study 3* (*Chapter 8*) showed that AmED typically dose-dependently decreased BrAC at peak intoxication and on the descending limb relative to alcohol without ED. This decrement in BrAC is likely attributable to the sugar content of EDs, with previous research suggesting that beverage carbohydrate content can slow alcohol absorption; whether these decrements in BrAC exceed those of other naturally-sweetened alcoholic mixers remains to be established. *Study 3* showed that participants rated their level of intoxication lower after co-ingesting a moderate alcohol dose with three standard 250mL EDs relative to having alcohol alone or with one or two standard 250mL EDs, even after controlling for BrAC differences. This effect was only evident at peak BrAC after a moderate alcohol dose, suggesting that the influence of ED on perceived intoxication may decrease at higher levels of

objective intoxication. This finding supports the theorised change in the intensity of intoxication post-AmED consumption. AmED-induced changes in perceived intoxication following moderate alcohol consumption may have implications for risk-taking behaviour, in particular drunk-driving, as the BrAC achieved when these results were observed reflect the legal drink-driving limit. This potential inverse causal link between decreased perceived intoxication and increased risk-taking following AmED consumption requires investigation. Furthermore, it remains to be seen whether the AmED-induced reductions in perceived intoxication materialise in the natural drinking environment.

9.6 Policy and Practical Implications

As reviewed in *Chapter 2*, there is an increasing body of epidemiological data (e.g., emergency department and poison information call centre cases) indicating rising rates of adverse exposures related to EDs co-ingested with other substances, primarily alcohol (Gunja & Brown, 2012; Substance Abuse and Mental Health Service Administration, 2011); whether this inflation parallels the increasing prevalence of AmED use remains to be established. However, the clinical severity of a proportion of these cases (A. J. Berger & Alford, 2009) indicates that further investigation as to the pharmacological effects of AmED is warranted. As noted earlier, EDs are relatively new beverages; the market-dominant ED, Red Bull®, was only released in the United States in 1997 (Reissig et al., 2009), with a subsequent introduction in Australia. The increasing popularity of mixed use, coupled with the emerging research outlined above, necessitates suggestions for harm reduction, as well as potential supply and demand reduction.

Currently, the relevant regulatory bodies in Australia outline recommended maximum daily intake guidelines for consumption of the two beverages independently. Retrospective self-report data from Australian AmED consumers in the present research indicates that these guidelines are typically exceeded when combining the two substances (*Chapter 3* and *4*). Whilst this consumer demographic typically report alcohol intake above and beyond the maximum amount outlined for harm reduction purposes in the National Health and Medical Research (2009) guidelines, it appears that, in situ, greater quantities of both constituents are ingested when mixed as compared to when consumed independently. Whether this intake reflects an informed decision to discount the guidelines or a lack of awareness is unknown; however, the increased odds of over-stimulation side-effects (e.g., heart palpitations, 'jolt and crash' episodes, sleeping difficulties) of an unknown clinical severity indicates the necessity of health promotion in both instances.

Food Standards Australia and New Zealand (2009) currently specifies that product packaging display an advisory statement recommending the maximum daily consumption volume. If future research assessing the clinical severity and dose-dependency of these side-effects aligns with the present outcomes, it may be that product packaging could be adapted to specify the potential side-effects of excess consumption. High volume products containing multiple serves (e.g., 1.25L bottles of ED containing five 250mL serves) which exceed the recommended maximum intake guidelines if ingested in one sitting may require more explicit warning labels. Furthermore, it may be that restrictions for sale of ED beverages that contain more than the recommended maximum daily intake mixed with alcohol (e.g., Red Bull® and vodka 'jugs' with a capacity for 1140mL) are required. Health promotion

messages could be integrated into existing alcohol awareness advertising campaigns (Australian National Preventive Health Agency), education resources (Alcohol and Drug Information Service, 2013), and school-based education programs implemented in some states and territories (Department of Education and Early Child Development, 2013). Highlighting potentially sensitive consumer groups and emphasising harm reduction by minimising intake could result in a more informed consumer, although evidence suggests that such information educational strategies might have limited efficacy as opposed to more direct intervention-based harm reduction measures (Foxcroft, Ireland, Lister-Sharp, Lowe, & Breen, 2003; Larimer & Cronce, 2002).

Retrospective self-report by consumers in the present research showed lower rates of risk-taking after AmED versus alcohol. In contrast, the experimental research provided mixed evidence in regards to the relative pharmacological effects of AmED versus alcohol on risky and impulsive behaviour, although potential issues with the sensitivity of this assessment and generalisability to real-life AmED consumption may underlie these outcomes. Whilst these results could be interpreted to suggest minimal reason for concern in regards to AmED-related risk-taking, the findings of the final study raise some potential issues for consumers. AmED-induced decreases in perceived intoxication after excess ED intake, even after controlling for differences in BrAC, may increase the risk of alcohol-related harm, in that consumers may perceive themselves as less intoxicated than indicated by their objective state, and consequently engage in behaviours (e.g., driving) which they are legally and/or physically unable to perform without harm to self or others. Previous research has shown that breath alcohol estimation training has limited success,

particularly when participants attempt to transfer learned skills to the natural drinking environment (Aston & Liguori, 2013). Consequently, health promotion regarding intake and intoxication and legislation reforms regarding sale and supply will be required if AmED-induced decreased perception of intoxication is: (i) replicated in experimental and field-based studies with greater statistical power, and (ii) shown to cause an increase in alcohol-related harms.

AmED consumers typically report greater pre-existing tendencies towards risk-taking relative to non-AmED consumers (Brache & Stockwell, 2011); the combination of trait risk-taking tendency and state-dependent increases in risk-taking after AmED consumption presents a high risk profile. The survey data from the present research showed that the majority of Australian consumers were ingesting AmED in licensed venues late at night. Legislative reform for availability in licensed venues has been enacted in some states of Australia, with sales of AmED beverages after midnight banned in licensed venues in Western Australia to minimise alleged AmED-related increases in alcohol-related violence and physical harm; the impact of these changes is currently being monitored. Research looking at the impact of controls on alcohol availability typically show that longer trading hours result in increased rates of drinking and alcohol-related harms (Chikritzhs & Stockwell, 2002; Popova, Giesbrecht, Bekmuradov, & Patra, 2009), presenting a promising picture for AmED sale restrictions.

There is also a strong body of research showing that population-based measures related to alcohol pricing policies, specifically increased taxation and restricted discounting practices, decrease alcohol use and negative health outcomes (Chisholm,

Rehm, Van Ommeren, & Monteiro, 2004; Purshouse, Meier, Brennan, Taylor, & Rafia, 2010), with consumers aged 18 to 24 years (within the target ED consumer age demographic of 18 to 34 years) most affected. These measures ensure that those who consume the most, and are consequently at the greatest risk of causing harm to self or others, have the greatest financial burden (Purshouse et al., 2010). Nearly half of Australian AmED consumers in *Study 1* reported that their AmED beverage choice was driven by drink-discounting, indicating that legislation regarding AmED pricing may be an effective countermeasure to reduce intake.

In sum, AmED-harms could be minimised via restrictions in licensed venues for: (i) the volume sold as one serve, (ii) late-night hours of sale, and (iii) discounted sales and promotions. However, overall, there are few definitive conclusions which can be drawn from the present studies, or from this field of research more broadly, regarding a *causal* link between AmED use and increased alcohol-related harms. Some researchers (Verster & Alford, 2011; Verster et al., 2012) have consequently claimed that potential harms experienced post-AmED consumption can only be attributed to excess alcohol intake, arguing that the ED component confers no additional harm, and that future harm minimisation endeavours should be targeted at the use and availability of alcohol in general. However, this doctoral research indicates that such conclusions may be premature; a lack of evidence showing a causal link between AmED use and alcohol-related harms does not necessarily equate to a lack of justifiable cause for concern. The aforementioned researchers (Verster & Alford, 2011; Verster et al., 2012) acknowledge the scarcity of research upon which to draw conclusions of AmED-related harms. However, the available clinical data suggests that AmED use is associated with some additional harms; the

lack of evidence clarifying whether these potential harms may be a direct consequence of the beverage itself or a consequence of a combination of factors (e.g., concomitant use of other substances, expectancy effects, drinking environment) does not preclude proactive action to maximise consumer safety.

9.7 Conclusion

The research reviewed in this thesis was undertaken to address questions regarding the practice of co-ingesting alcohol and ED, and to provide an evidence base for policy reform and consumer awareness programs regarding the potential harms of use. Overall, the results of the present research suggest that AmED consumption may alter the nature and intensity of intoxication, but that these effects may be dependent on the volume of the alcohol and ED dose, as well as other non-pharmacological factors. Definitive conclusions as to whether these AmED-induced changes translate into additional alcohol-related adverse behavioural outcomes are precluded due to conflicting outcomes in the current research. This fact, coupled with the general lack of research in this area, limits policy reform and consumer education endeavours. However, this research forms an initial foundation for building an evidence base regarding these issues; replication of the outcomes and systematic manipulation and assessment of pharmacological and non-pharmacological factors could clarify the public health approach to this popular consumption trend.

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Appendix A: Systematic Review Study Protocol

CONFIDENTIAL

Systematic Review Protocol

'High' Risk? A Systematic Review of the Acute Outcomes of Mixing Alcohol with Energy Drinks

Date: April 2013

Version: 1.

A1. General Information

A1.1 Research Team

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A2. Synopsis

Study Title: 'High' Risk? A Systematic Review of the Acute Outcomes of Mixing Alcohol with Energy Drinks

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Anticipated Start Date: 1 May 2013

Anticipated Completion Date: 1 November 2013

Funding Sources: None.

Conflicts of Interest: Peacock and Bruno were provided placebo samples by Red Bull GmBH in a prior experimental study; no financial support was provided and this organisation had no involvement in design, interpretation, or reporting of the previous work. Red Bull GmBH have no involvement in the proposed manuscript.

Dr Lubman has received speaker fees from AstraZeneca and Janssen, and provided consultancy advice to Lundbeck. The researchers have no other connections with the tobacco, alcohol, pharmaceutical or gaming industries, or any body substantially funded by one of these organisations.

A3. Background

Alcohol-related problems, particularly those associated with the night-time economies of urban and regional centres, are the subject of substantial community concern across Australia. While the number of people drinking in Australia appears to be declining (Australian Institute of Health and Welfare, 2011), and population levels of consumption appear stable (World Health Organisation, 2004), there have been increases over time in alcohol-attributable hospitalisations in most jurisdictions across Australia and these increases are independent of an overall increase in hospitalisations over time. One explanation for this may be the nature of alcohol consumption by young people in the night-time economy, with national data indicating that almost one third of 18-29 year olds consume alcohol above National Health and Medical Research Council thresholds for 'risky drinking' weekly, and over half do so monthly (Australian Institute of Health and Welfare, 2011). It is therefore no surprise that alcohol is consistently associated with injury and violence among young people of this age group.

A recent consumption trend associated with additional alcohol-related harms is the mixing of alcohol with energy drinks (AmED) (Pennay et al., 2011). The combination of AmED can be achieved by purchasing pre-mixed beverages, hand-mixing the two constituents, or consuming the two beverages separately in a drinking session. International studies targeting adolescent and young adult samples, key risk groups for high-risk drinking, indicate widespread use (Brache & Stockwell, 2011; Oteri et al., 2007). While few studies have been conducted examining AmED use in Australia, a community-based survey of a convenience sample revealed that nearly half (46%, *n*=403) of Australian participants aged 18-35 years had used

AmED in the previous six months (Peacock et al., 2012). Such results suggest that AmED use among Australian youth is becoming normative.

AmED use amongst this high-risk demographic has generated considerable concern amongst researchers, health professionals, and policy-makers in regards to the additional acute adverse health outcomes. The practice of co-ingesting a stimulant (energy drink) with a depressant (alcohol) is thought to directly impact on the consumer's experience of intoxication, masking the depressant physiological and psychological side-effects of alcohol and increasing the experience of side-effects related to over-stimulation. Concerns regarding the additional harmful side-effects of AmED use have been amplified following media reports of extreme physiological and psychological adverse reactions and, in a few cases, fatalities, following AmED consumption. Certain physiological and psychological outcomes are proposed to be more likely following AmED relative to alcohol consumption due to the oppositional global pharmacological effects of the two constituents.

These physiological and psychological changes following AmED consumption are also thought to be coupled with behavioural changes, specifically increased engagement in hazardous drinking practices and other risky behaviours. It is thought that AmED creates a state of 'wide-awake drunkenness', whereby consumers report lower intoxication relative to when consuming alcohol alone (Arria & O'Brien, 2011). This misperception of intoxication may result in greater alcohol intake and poorer decision-making and risk assessment. The possibility of increased alcohol intake, coupled with an increased propensity towards risk-taking, heightens the risk of alcohol-related harms, including driving while intoxicated, engaging in

disinhibited behaviour, such as physical and verbal abuse (leading to fights and assaults), or being injured following a fall or accident.

The Australian Medical Association has released several public reports highlighting the dangers of AmED consumption and called repeatedly for review of energy drink and AmED marketing and limits on consumption (Australian Medical Association, December, 2010). Similarly, the European Centre for Monitoring Alcohol Marketing, the National Foundation for Alcohol Prevention in the Netherlands, Food Safety Promotion Board of the Republic of Ireland, and the Canadian Centre on Substance Abuse have called for further regulation of energy drinks and AmED (Anderson, 2007; European Centre for Monitoring Alcohol Marketing, 2008; Food Safety Promotion Board), while the US Food and Drug Administration has released consumer updates outlining health concerns surrounding AmED use (United States Food and Drug Administration, November, 2010). In Australia, the Ministerial Council on Drug Strategy have tasked the Intergovernmental Committee on Drugs to develop an urgent action plan to address the increasing harms from AmED consumption. This attention, and the increasing prevalence of AmED use, has seen an exponential growth in the research on the physiological, psychological and behavioural acute harms of AmED use. However, there have been no recent attempts to formally and objectively synthesise the data outlining the health harms of AmED use. A systematic and impartial review of the literature regarding the health effects of AmED consumption is necessary to provide a strong evidence base for any changes to current policy.

As such, the primary objective of this review will be to summarise the self-report and objective data regarding the effects of combining AmED. This review will focus on AmED-induced changes in consumers' physiological and psychological state and behavioural state, particularly in regards to alcohol intake and other risk-taking behaviours.

A4. Methodology

A4.1 Inclusion and Exclusion Criteria

A4.1.1 Publication Criteria

This review will consider all studies that quantitatively measure the acute effects of AmED consumption. Studies adopting descriptive, observational analytic, and human experimental designs will be included; animal studies, case studies, qualitative papers, reviews, methodology papers, and commentaries will be excluded.

Articles published in languages other than English or prior to 1990 will be excluded. No publication status restrictions will be imposed.

A4.1.2 Content Criteria

For the purposes of this study, an ED is defined as a functional beverage marketed as facilitating attention and endurance. The primary ED constituents are caffeine, sugars, and taurine. Other potential ingredients of EDs may include glucuronolactone, B vitamins and herbal extracts. Studies will be excluded if they report the effects of an energy beverage which does not contain all the primary ingredients stated above.

AmED use will be defined as co-ingestion of ED and alcohol via:

- Consumption of pre-mixed beverages containing the two constituents
- Consumption of hand-mixed beverages containing the two constituents
- Consumption of the two constituents as separate beverages within the same drinking session.

As the objective will be to examine the relative likelihood of harms after AmED and alcohol, articles will be included if they report a comparison of AmED versus alcohol consumers (between-subjects), or AmED versus alcohol consumption (within-subjects) in regards to: (i) physiological, psychological, cognitive and psychomotor outcomes, (ii) alcohol consumption and alcohol priming, or (iii) risk-taking behaviour.

A4.2 Search Source(s)

Electronic searching strategies will be used to identify studies.

Online databases PubMed/Medline, PsycINFO, and Embase will be searched for journal articles published in English between 1/1/1990 and the first search date. In order to identify AmED publications, the alcohol-related search term (alcohol*) will be used in combination with the energy drink-related search terms (“energy drink*”, “Red Bull”) using the Boolean operator ‘and’. As the combination of AmED terms may yield a large number of returns, a targeted search will be undertaken, with each of the alcohol and ED search term combinations used in conjunction with search terms specific to the harms of use: risk*, behavio*, adverse*, effect*, harm*,

health*, excess*, consum*, intake*. All studies including these terms in the title and/or abstract will be retrieved.

A4.3 Selection Procedure

The primary reviewer will undertake the search for sources. A search diary will be maintained detailing the names of the databases searched, the keywords used, and the number of search results. Titles and abstracts of studies will be recorded in an EndNote database, along with details as to where the reference was found. Any duplicates of records will be removed by the primary reviewer. Any articles that are obviously unsuitable on the basis of the publication criteria will be excluded in the early stages of the search by the primary reviewer based on title and abstract. Content assessment (based on title/abstract) will be performed by two reviewers using a standardised template, with full-texts sought where required by the reviewer. The reviewers will not be blinded to the names of the authors, their institutions, and journals of publication. The number of records remaining after each stage will be detailed, and the reasons for exclusion, and the exclusion stage, will be documented in the citation record. Disagreement between the reviewers regarding inclusion will be overcome by consensus following discussion of the articles; a third reviewer will be asked to blindly assess the relevance of the article in the event that a consensus is not reached.

A4.4 Data Extraction

Articles will be grouped according to the research question(s) addressed. The primary details extracted will include the study aim, design, sample characteristics, sampling method, primary measures, method of administration, outcomes,

conclusions, limitations, funding, and conflicts of interest. Data will be extracted independently by the primary and secondary reviewer. Authors will be contacted in the event of missing information/data; failure to respond will result in the data being coded as missing.

A4.5 Study Quality Assessment

The following measures will be used to assess study quality:

- The Joanna Briggs Institute Critical Appraisal Checklist for Descriptive Studies (Joanna Briggs Institute, 2011)
- Joanna Briggs Critical Appraisal Criteria for Cohort/Case-Control Studies (Joanna Briggs Institute, 2011)
- Cochrane Collaboration tool (Higgins et al., 2011)

Studies will not be excluded on the basis of quality although the data collected in this process will be used for the qualitative review.

A4.6 Strategy for Data Synthesis

Odds ratios (OR) will be calculated based on reported descriptive and inferential statistics. Outcomes will be grouped within each theme area as: (i) self-reported drinking outcomes in natural scenarios (retrospective or prospective) for (a) AmED versus alcohol consumers, and (b) AmED versus alcohol sessions, (ii) self-reported outcomes of AmED versus alcohol administration in laboratory-based settings, and (iii) objective outcomes of AmED versus alcohol administration in laboratory-based settings.

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Appendix B: Systematic Review Example Search Strategy

B1. PsycINFO Search Strategy

1. ab,ti(Alcohol* AND “energy drink*” AND risk*)
2. ab,ti(Alcohol* AND “energy drink*” AND behavio*)
3. ab,ti(Alcohol* AND “energy drink*” AND effect*)
4. ab,ti(Alcohol* AND “energy drink*” AND adverse*)
5. ab,ti(Alcohol* AND “energy drink*” AND harm*)
6. ab,ti(Alcohol* AND “energy drink*” AND health*)
7. ab,ti(Alcohol* AND “energy drink*” AND excess*)
8. ab,ti(Alcohol* AND “energy drink*” AND consum*)
9. ab,ti(Alcohol* AND “energy drink*” AND intake*)
10. ab,ti(Alcohol* AND “Red Bull*” AND risk*)
11. ab,ti(Alcohol* AND “Red Bull*” AND behavio*)
12. ab,ti(Alcohol* AND “Red Bull*” AND effect*)
13. ab,ti(Alcohol* AND “Red Bull*” AND adverse*)
14. ab,ti(Alcohol* AND “Red Bull*” AND harm*)
15. ab,ti(Alcohol* AND “Red Bull*” AND health*)
16. ab,ti(Alcohol* AND “Red Bull*” AND excess*)
17. ab,ti(Alcohol* AND “Red Bull*” AND consum*)
18. ab,ti(Alcohol* AND “Red Bull*” AND intake*

Appendix C: Survey of Alcohol and Energy Drink Use (Study 1)

Survey of Alcohol and Energy Drink Use

Research conducted at the School of Psychology, University of Tasmania by Amy Peacock, Associate Professor Frances Martin, and Dr Raimondo Bruno

Thank you for your interest in participating in this study

INFORMATION SHEET
Survey of Alcohol and Energy Drinks

This study is being conducted by Amy Peacock in partial fulfilment of the requirements of a PhD in the School of Psychology, University of Tasmania. Amy is supervised by Associate Professor Frances Martin and Dr Raimondo Bruno from the School of Psychology, University of Tasmania.

What is the purpose of the study?

The purpose of this study is to investigate the prevalence, consumption patterns, motivations for, and consequences of, alcohol and energy drink use.

Who can participate?

You are eligible to participate in this study if you are at least 18 years of age. You do not have to drink energy drinks and/or alcohol to be eligible to participate.

What does this study involve?

Participation involves completing a 10-30 minute survey electronically (https://surveys.psychol.utas.edu.au). There will be questions in the survey about your history of, and current, alcohol and energy drink use, specifically examining the motivations for and consequences of use. At the end of the survey you will be asked if you would like to be contacted to participate in further research, which would involve coming to the Cognitive Neuroscience Laboratory at the University of Tasmania and taking part in cognitive processing experiments.

Are there any benefits of participating?

To thank you for your participation, you may enter a prize draw to win an Apple iPad 2 on completing the survey. Additionally, your participation will increase understanding as to why people consume alcohol and energy drinks. This information will be used to help educate people regarding the potential motivations for, and outcomes of, alcohol and energy drink use.

Are there any possible risks associated with participating?

There are no specific anticipated risks of completing this survey. However, if you find you become distressed or feel uncomfortable while completing the survey, please stop the survey and seek assistance from Lifeline on 131114. Lifeline is a telephone counselling, support and information referral service which operates 24 hours a day, 7 days a week in Australia. You could also contact Counselling Online (http://www.counsellingonline.org.au/en/); Alcoholics Anonymous (Hobart: 03 6234 8711, Launceston: 03 6334 7060, http://www.aa.org.au/), or SANE (1800 18 7263 or http://www.sane.org/) if you wish.

How private is the information that I give?

All information will be kept confidential and you will not be required to give your name or contact details. If you decide to enter the prize draw and/or volunteer to participate in further research, your contact details will be stored separately to your survey responses. All data will be stored on password protected secure computers in the School of Psychology for a minimum of five years after the publication of any academic journal articles, at which point all questionnaire data will deleted.

How do I consent to participate? Can I withdraw from the research if I wish?

Participation is voluntary. By submitting your completed questionnaire, you are indicating that you are aware of the nature of the study from reading the information sheet and that you wish to participate. While we would be pleased to have you participate, we respect your right to decline. Each item is optional; please feel free to skip any questions you perceive as distressing or sensitive. If you decide to discontinue participation at any time, you may do so without providing an explanation.

Who do I contact if I have any questions?

Please feel free to copy or print this information sheet. If you would like to discuss any aspect of this study please contact Amy Peacock on (03) 6226 7458 or email Amy.Peacock@utas.edu.au. Alternatively, you can contact Associate Professor Frances Martin on (03) 6226 2262 or email Frances.Martin@utas.edu.au.

Has this research been approved by an ethics committee?

This study has been approved by the Tasmanian Social Science Human Research Ethics Committee. If you have concerns or complaints about the conduct of this study should contact the Executive Officer of the HREC (Tasmania) Network on (03) 6226 7479 or email human.ethics@utas.edu.au. The Executive Officer is the person nominated to receive complaints from research participants. You will need to quote H0011734.

How do I find out about the results of the study?

The findings of this study will be available via the University of Tasmania School of Psychology website (http://fcms.its.utas.edu.au/scieng/psychol/) and promoted in the Tasmanian news media in 2011/2012. Results of the study can also be provided by Amy Peacock ((03) 6226 7458 or email Amy.Peacock@utas.edu.au).

Your completion and submission of the survey constitutes your consent to participate in this study. Please feel free to print or copy this information sheet for later reference. If you are still interested in participating, please click 'Next'

Screening Question 1: Are you at least 18 years of age?

No ..... 0 *(Redirect)*
Yes ..... 1 *(Go to Screening Question 2)*

Screening Question 2: Have you drunk an energy drink in the last 6 months?

No ..... 0 *(Skip to Screening Question 3)*
Yes ..... 1 *(Go to Section A)*

1. The following questions ask about your use of energy drinks in the *last 6 months*. Please refer to the fact sheet showing standard energy drink sizes to help with your estimation.

How often do you drink an energy drink?	Never *(Skip to Inclusion Question 2)*	Monthly or less	2 to 4 times a month	2 to 3 times a week	4 or more times a week
How many standard energy drinks do you have on a typical day when you are drinking energy drink(s)?	_____ standard energy drink(s)				
How often do you drink three or more standard energy drinks in a single day?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily
What is the greatest number of standard energy drinks you have consumed in a single day?	_____ standard energy drink(s)				

Screening Question 3: Have you drunk an alcoholic drink in the last 6 months?

No ..... 0 *(Skip to Screening Question 4)*
Yes ..... 1 *(Go to Section B)*

1. The following questions ask about your use of alcohol in the *last 12 months*. Please refer to the fact sheet showing standard alcohol drink sizes to help with your estimation. All information provided will be kept confidential.

How often do you have a drink containing alcohol?	Never *(Skip to Inclusion Question 4)*	Monthly or less	2 to 4 times a month	2 to 3 times a week	4 or more times a week
How many standard drinks containing alcohol do you have on a typical day when you are drinking?	1 or 2	3 or 4	5 or 6	7 to 9	10 or more
How often do you have six or more standard drinks on one occasion?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily
How often during the last year have you found that you were not able to stop drinking once you had started?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily
How often during the last year have you failed to do what was normally expected of you because of drinking?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily
How often during the last year have you needed a first drink in the morning to get yourself going after a heavy drinking session?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily
How often during the last year have you had a feeling of guilt or remorse after drinking?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily
How often during the last year have you been unable to remember what happened the night before because of your drinking?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily
Have you or someone else ever been injured because of your drinking?	No		Yes, but not in the last year		Yes, during the last year
Has a relative or friend or a doctor or other health worker, ever been concerned about your drinking or suggested you cut down?	No		Yes, but not in the last year		Yes, during the last year

2. The following questions ask about your use of alcohol in the *past 30 days*. Please note that a drinking session refers to a period of time when you were continuously under the influence of alcohol.	
On how many of the past 30 days did you have a drink containing alcohol?	____day(s)
In the past 30 days, how many standard alcoholic drinks did you have in a typical drinking session?	____standard alcoholic drink(s)
In how many drinking sessions in the past 30 days did you drink two or more standard alcoholic drinks?	____drinking session(s)
In the past 30 days, what was the greatest number of standard alcoholic drinks you consumed in a single drinking session?	____standard alcoholic drink(s)

Screening Question 4: In the last 6 months, have you drunk an alcoholic drink AND an energy drink in the same drinking session?

No ..... 0 *(Skip to Section E)*
Yes ..... 1 *(Go to Section C)*

The next section contains questions about your use of energy drinks and alcohol together in a drinking session during the *past 6 months*. Please note that a drinking session refers to a period of time when you were continuously under the influence of alcohol and/or energy drinks.

1. In the past 6 months, how frequently did you drink an energy drink AND an alcoholic drink in the same drinking session?

Never ..... 0 (Skip to Section E)
Monthly or less 1
2 to 4 times per month 2
2 to 3 times per week 3
4 or more times per week 4

2. How many standard alcoholic drinks AND standard energy drinks did you have the last time you drank alcohol AND energy drinks in a single drinking session? *A fact sheet showing standard alcoholic drink sizes and standard energy drink sizes is available to help with your estimation.*

_____ standard alcoholic drinks

_____standard energy drinks

3. In the last 6 months, what was the greatest number of standard alcoholic drinks AND standard energy drinks you had in a single drinking session?

_____ standard alcoholic drinks

_____ standard energy drinks

4. Alcohol and energy drinks can be used together in two ways: (1) mixed together in one drink, or (2) drunk as separate drinks in the one drinking session. In the last 6 months, did you typically:

Mix energy drink(s) and alcohol together in one drink ..... 1 *(Go to Q7)*
Drink the energy drink(s) and alcoholic drink(s) as separate drinks ... 2 *(Skip to Q5)*

5. In the last 6 months, how many minutes typically passed between you finishing an alcoholic drink and starting an energy drink (or finishing an energy drink and starting an alcoholic drink) in a drinking session?

_____ minute(s) *(Skip to Section C11 for those who answered 2 above)*

6. In a typical drinking session in the last 6 months when you were ***mixing* alcohol AND energy drinks, how many of your drinks were a mix of alcohol and energy drink(s)?**

None 0
Less than half 1
Half 2
More than half 3
All 4

7. In the last 6 months, what types of alcohol have you mixed with energy drinks? *(Mark all relevant responses)*

Spirits (e.g., vodka, gin, rum) 1
Beer 2
Wine 3
Champagne 4
Liqueur (e.g., chartreuse, AGWA, jagermeister) 5

8. In the last 6 months, what was your favourite or preferred type of alcohol to mix with energy drinks? *(Mark one response)*

Spirits (e.g., vodka, gin, rum) ..... 1 *Go to Q9*
Beer ..... 2 *Skip to Q10*
Wine ..... 3 *Skip to Q10*
Champagne ..... 4 *Skip to Q10*
Liqueur (e.g., chartreuse, AGWA, jagermeister) ..... 5 *Skip to Q10*

9. In the last 6 months, which alcoholic spirit did you typically mix with energy drinks?

Vodka 1
Gin 2
Whisky 3
Tequila 4
Brandy 5
Rum 6
Absinthe 7
Other ..... 8 **Specify**__

10. In the last 6 months, which energy drink did you typically mix with alcohol?

Red Bull 1
Red Bull Sugarfree 2
Monster 3
Mother 4
V 5
Rockstar 6
Other ..... 7 **Specify**__

11. In the last 6 months, what time of day did you typically *start* drinking alcohol and energy drinks together (either mixed together or drunk as separate drinks)? *(Mark one response)*

12:01am– 3:00am	1
3:01am – 6:00am	2
6:01am - 9:00am	3
9:00am –Midday	4
12:01pm – 3:00pm	5
3:01pm – 6:00pm	6
6:01pm – 9pm	7
9:01pm – Midnight	8

12. In the last 6 months, where did you spend most of your time when you were drinking alcohol and energy drinks together (either mixed together or drunk as separate drinks)?

Home	1
Nightclub	2
Party	3
Bar/pub	4
Public place (street/park)	5
Live music event*	6
Work/university/school	7
Playing sport/exercising	8
Other	9 **Specify**_____

**concerts, music festivals*

13. In how many of all your alcohol drinking sessions in the last 6 months did you drink at least one energy drink with alcohol (either mixed together or as separate drinks)?

None	0
Less than half	1
Half	2
More than half	3
All	4

14. In the last six months, did you typically drink energy drinks with alcohol ((either mixed together or drunk as separate drinks) when you were planning to have a normal drinking session, or when you were planning to have a heavy drinking session?

Normal drinking session	1
Heavy drinking session	2

1. Below are a number of statements that describe reasons why people may drink energy drinks with alcohol (either mixed together or consumed as separate drinks). Please indicate how frequently the following reasons motivated you to drink energy drinks with alcohol *in the last 6 months.*

I drank energy drinks with alcohol...

Because I like the taste of alcohol and energy drinks together	Never	Less than half the time	Half the time	More than half the time	All the time
To avoid getting a hangover	Never	Less than half the time	Half the time	More than half the time	All the time
So I could stay out later	Never	Less than half the time	Half the time	More than half the time	All the time
Because energy drinks were available to drink with alcohol	Never	Less than half the time	Half the time	More than half the time	All the time
To have more fun	Never	Less than half the time	Half the time	More than half the time	All the time
To feel less drunk	Never	Less than half the time	Half the time	More than half the time	All the time
As a legal alternative to illegal drugs	Never	Less than half the time	Half the time	More than half the time	All the time
To hide the flavour of alcohol	Never	Less than half the time	Half the time	More than half the time	All the time
To feel more energetic	Never	Less than half the time	Half the time	More than half the time	All the time
So I could drink more	Never	Less than half the time	Half the time	More than half the time	All the time
To look less drunk	Never	Less than half the time	Half the time	More than half the time	All the time
Because I like the combined effect	Never	Less than half the time	Half the time	More than half the time	All the time
Because it was available at a party	Never	Less than half the time	Half the time	More than half the time	All the time
Because they are ingredients in a drink (i.e. Jagerbomb, Red Bull vodka)	Never	Less than half the time	Half the time	More than half the time	All the time

I drank energy drinks with alcohol...	Never	Less than half the time	Half the time	More than half the time	All the time
Because I like the taste of energy drinks	o	o	o	o	o
To get a bigger buzz	o	o	o	o	o
To feel more confident	o	o	o	o	o
To be more alert	o	o	o	o	o
Because other people I knew were drinking them	o	o	o	o	o
To simulate or mimic the effects of illegal drugs (e.g., ecstasy)	o	o	o	o	o
To be able to concentrate more	o	o	o	o	o
To feel more sociable	o	o	o	o	o
Because energy drinks are a popular drink to mix with alcohol	o	o	o	o	o
To improve my mood	o	o	o	o	o
For the thrill	o	o	o	o	o
Because there was a discount drink special	o	o	o	o	o
To decrease boredom	o	o	o	o	o
For something different to drink	o	o	o	o	o
Because I can drink them together quickly	o	o	o	o	o
To get more drunk	o	o	o	o	o
Because someone bought it for me	o	o	o	o	o
Because the person/group of people I was with were drinking them (e.g., had shots together, shared a jug of alcohol and energy drink mixed together)	o	o	o	o	o

2. Below are a number of behaviours people may display while drinking alcohol alone AND/OR while drinking energy drinks with alcohol (either mixed together or drunk as separate drinks). Please indicate whether you have done the following *in the last 6 months* while: **(1) drinking alcohol alone** **(2) drinking energy drinks with alcohol.** ***Some of the following questions are of a sensitive nature. Please remember that your data is not personally identifiable and will be kept confidential.***			
I was asked to leave or kicked out of a club/bar/pub	No, I haven't while drinking alcohol only	*Skip to next*	
	Yes, while I was drinking alcohol only	*Skip to next*	
	No, I haven't while drinking energy drinks with alcohol	*Skip to next*	
	Yes, while I was drinking energy drinks with alcohol	To what extent do you believe that you being asked to leave or being kicked out of a club/bar/pub was due to you drinking energy drinks with alcohol?	Not at all Somewhat Mostly All
I was a passenger in a vehicle being driven by someone who was probably/definitely over the legal alcohol limit for driving	No, I haven't while drinking alcohol only	*Skip to next*	
	Yes, while I was drinking alcohol only	*Skip to next*	
	No, I haven't while drinking energy drinks with alcohol	*Skip to next*	
	Yes, while I was drinking energy drinks with alcohol	To what extent do you believe that you being a passenger in a vehicle being driven by someone probably/definitely over the legal alcohol limit for driving was due to you drinking energy drinks with alcohol?	Not at all Somewhat Mostly All

I spent more money than I planned to	No, I haven't while drinking alcohol only	*Skip to next*	
	Yes, while I was drinking alcohol only	*Skip to next*	
	No, I haven't while drinking energy drinks with alcohol	*Skip to next*	
	Yes, while I was drinking energy drinks with alcohol	To what extent do you believe that you spending more money than you planned to was due to you drinking energy drinks with alcohol?	Not at all Somewhat Mostly All
I acted on a dare which had the potential to cause harm to myself and/or others	No, I haven't while drinking alcohol only	*Skip to next*	
	Yes, while I was drinking alcohol only	*Skip to next*	
	No, I haven't while drinking energy drinks with alcohol	*Skip to next*	
	Yes, while I was drinking energy drinks with alcohol	To what extent do you believe that you acting on a dare which had the potential to cause harm to yourself or others was due to you drinking energy drinks with alcohol?	Not at all Somewhat Mostly All
I had a verbal fight with someone (e.g., shouted, screamed, swore)	No, I haven't while drinking alcohol only	*Skip to next*	
	Yes, while I was drinking alcohol only	*Skip to next*	
	No, I haven't while drinking energy drinks with alcohol	*Skip to next*	
	Yes, while I was drinking energy drinks with alcohol	To what extent do you believe that you having a verbal fight with someone was due to you drinking energy drinks with alcohol?	Not at all Somewhat Mostly All

I had sex with someone I had only recently met	No, I haven't while drinking alcohol only	*Skip to next*	
	Yes, while I was drinking alcohol only	*Skip to next*	
	No, I haven't while drinking energy drinks with alcohol	*Skip to next*	
	Yes, while I was drinking energy drinks with alcohol	To what extent do you believe you having sex with someone you had only recently met was due to you drinking energy drinks with alcohol?	Not at all Somewhat Mostly All
I did not wear a seatbelt while I or someone else was driving a vehicle	No, I haven't while drinking alcohol only	*Skip to next*	
	Yes, while I was drinking alcohol only	*Skip to next*	
	No, I haven't while drinking energy drinks with alcohol	*Skip to next*	
	Yes, while I was drinking energy drinks with alcohol	To what extent do you believe that you not wearing a seatbelt while you or someone else was driving a vehicle was due to you drinking energy drinks with alcohol?	Not at all Somewhat Mostly All
I did not use contraception (e.g., condom/glove) while having sex with someone	No, I haven't while drinking alcohol only	*Skip to next*	
	Yes, while I was drinking alcohol only	*Skip to next*	
	No, I haven't while drinking energy drinks with alcohol	*Skip to next*	
	Yes, while I was drinking energy drinks with alcohol	To what extent do you believe that not using contraception while having sex was due to you drinking energy drinks with alcohol?	Not at all Somewhat Mostly All

I was in vehicle with an illegal number of passengers (e.g., 6 people in a 5 seater car)	No, I haven't while drinking alcohol only	*Skip to next*	
	Yes, while I was drinking alcohol only	*Skip to next*	
	No, I haven't while drinking energy drinks with alcohol	*Skip to next*	
	Yes, while I was drinking energy drinks with alcohol	To what extent do you believe that you being in a car with an illegal number of passengers was due to you drinking energy drinks with alcohol?	Not at all Somewhat Mostly All
I was physically hurt or injured	No, I haven't while drinking alcohol only	*Skip to next*	
	Yes, while I was drinking alcohol only	*Skip to next*	
	No, I haven't while drinking energy drinks with alcohol	*Skip to next*	
	Yes, while I was drinking energy drinks with alcohol	To what extent do you believe that being physically hurt or injured was due to you drinking energy drinks with alcohol?	Not at all Somewhat Mostly All
I grabbed, pushed, slapped, punched and/or shoved someone	No, I haven't while drinking alcohol only	*Skip to next*	
	Yes, while I was drinking alcohol only	*Skip to next*	
	No, I haven't while drinking energy drinks with alcohol	*Skip to next*	
	Yes, while I was drinking energy drinks with alcohol	To what extent do you believe that you grabbing, pushing, slapping, punching or shoving someone was due to you drinking energy drinks with alcohol?	Not at all Somewhat Mostly All

I vandalised and/or intentionally destroyed property (e.g., drew graffiti, broke a window, damaged a car)	No, I haven't while drinking alcohol only	*Skip to next*	
	Yes, while I was drinking alcohol only	*Skip to next*	
	No, I haven't while drinking energy drinks with alcohol	*Skip to next*	
	Yes, while I was drinking energy drinks with alcohol	To what extent do you believe that you vandalising and/or intentionally destroying was due to you drinking energy drinks with alcohol?	Not at all Somewhat Mostly All
I was cautioned, restrained, charged, and /or fined by the police	No, I haven't while drinking alcohol only	*Skip to next*	
	Yes, while I was drinking alcohol only	*Skip to next*	
	No, I haven't while drinking energy drinks with alcohol	*Skip to next*	
	Yes, while I was drinking energy drinks with alcohol	To what extent do you believe you being cautioned, restrained, charged, and/or fined by the police was due to you drinking energy drinks with alcohol?	Not at all Somewhat Mostly All
I gambled	No, I haven't while drinking alcohol only	*Skip to next*	
	Yes, while I was drinking alcohol only	*Skip to next*	
	No, I haven't while drinking energy drinks with alcohol	*Skip to next*	
	Yes, while I was drinking energy drinks with alcohol	To what extent do you believe that you gambling was due to you drinking energy drinks with alcohol?	Not at all Somewhat Mostly All

I smoked cigarette(s)	No, I haven't while drinking alcohol only	*Skip to next*	
	Yes, while I was drinking alcohol only	*Skip to next*	
	No, I haven't while drinking energy drinks with alcohol	*Skip to next*	
	Yes, while I was drinking energy drinks with alcohol	To what extent do you believe that you smoking cigarettes was due to you drinking energy drinks with alcohol?	Not at all Somewhat Mostly All
I drank more alcohol than I planned to	No, I haven't while drinking alcohol only	*Skip to next*	
	Yes, while I was drinking alcohol only	*Skip to next*	
	No, I haven't while drinking energy drinks with alcohol	*Skip to next*	
	Yes, while I was drinking energy drinks with alcohol	To what extent do you believe that you drinking more alcohol than you planned to was due to you drinking energy drinks with alcohol?	Not at all Somewhat Mostly All
I used legal drugs (not including alcohol or cigarettes) or prescription medication for recreational purposes	No, I haven't while drinking alcohol only	*Skip to next*	
	Yes, while I was drinking alcohol only	*Skip to next*	
	No, I haven't while drinking energy drinks with alcohol	*Skip to next*	
	Yes, while I was drinking energy drinks with alcohol	To what extent do you believe that you using legal drugs or prescription medication for recreational purposes was due to you drinking energy drinks with alcohol?	Not at all Somewhat Mostly All

I acted in a way that resulted in me experiencing humiliation or embarrassment	No, I haven't while drinking alcohol only	*Skip to next*	
	Yes, while I was drinking alcohol only	*Skip to next*	
	No, I haven't while drinking energy drinks with alcohol	*Skip to next*	
	Yes, while I was drinking energy drinks with alcohol	To what extent do you believe that you acting in way that resulting in you experiencing humiliation or embarrassment was due to you drinking energy drinks with alcohol?	Not at all Somewhat Mostly All
I was touched in a sexual way and/or kissed by someone when I did not want them to	No, I haven't while drinking alcohol only	*Skip to next*	
	Yes, while I was drinking alcohol only	*Skip to next*	
	No, I haven't while drinking energy drinks with alcohol	*Skip to next*	
	Yes, while I was drinking energy drinks with alcohol	*Skip to next*	
I was in a vehicle exceeding the speed limit by at least 10% (e.g., driving 110 km per hour in a 100 km per hour zone)	No, I haven't while drinking alcohol only	*Skip to next*	
	Yes, while I was drinking alcohol only	*Skip to next*	
	No, I haven't while drinking energy drinks with alcohol	*Skip to next*	
	Yes, while I was drinking energy drinks with alcohol	To what extent do you believe that you being in a vehicle exceeding the speed limit by at least 10% was due to you drinking energy drinks with alcohol?	Not at all Somewhat Mostly All

I required emergency medical treatment	No, I haven't while drinking alcohol only	*Skip to next*	
	Yes, while I was drinking alcohol only	*Skip to next*	
	No, I haven't while drinking energy drinks with alcohol	*Skip to next*	
	Yes, while I was drinking energy drinks with alcohol	To what extent do you believe that you requiring emergency medical treatment was due to you drinking energy drinks with alcohol?	Not at all Somewhat Mostly All
I acted in a way that resulted in me experiencing guilt (e.g., something that I felt the need to apologise for)	No, I haven't while drinking alcohol only	*Skip to next*	
	Yes, while I was drinking alcohol only	*Skip to next*	
	No, I haven't while drinking energy drinks with alcohol	*Skip to next*	
	Yes, while I was drinking energy drinks with alcohol	To what extent do you believe that you acting in a way that resulted in you experiencing guilt was due to you drinking energy drinks with alcohol?	Not at all Somewhat Mostly All
I used illegal drugs (e.g., cannabis, ecstasy, speed, cocaine)	No, I haven't while drinking alcohol only	*Skip to next*	
	Yes, while I was drinking alcohol only	*Skip to next*	
	No, I haven't while drinking energy drinks with alcohol	*Skip to next*	
	Yes, while I was drinking energy drinks with alcohol	To what extent do you believe you using illegal drugs was due to you drinking energy drinks with alcohol?	Not at all Somewhat Mostly All

I drove a vehicle when I was probably/definitely over the legal alcohol limit for driving	No, I haven't while drinking alcohol only	*Skip to next*	
	Yes, while I was drinking alcohol only	*Skip to next*	
	No, I haven't while drinking energy drinks with alcohol	*Skip to next*	
	Yes, while I was drinking energy drinks with alcohol	To what extent do you believe you driving a vehicle when you were probably/definitely over the legal alcohol limit for driving was due to you drinking energy drinks with alcohol?	Not at all Somewhat Mostly All
I touched someone in a sexual way and/or kissed someone when they did not want me to	No, I haven't while drinking alcohol only	*Skip to next*	
	Yes, while I was drinking alcohol only	*Skip to next*	
	No, I haven't while drinking energy drinks with alcohol	*Skip to next*	
	Yes, while I was drinking energy drinks with alcohol	To what extent do you believe that you touching someone in a sexual way and/or kissing someone when they did not want you to was due to you drinking energy drinks with alcohol?	Not at all Somewhat Mostly All
I passed out (i.e., blacked out or lost consciousness)	No, I haven't while drinking alcohol only	*Skip to next*	
	Yes, while I was drinking alcohol only	*Skip to next*	
	No, I haven't while drinking energy drinks with alcohol	*Skip to next*	
	Yes, while I was drinking energy drinks with alcohol	To what extent do you believe that you passing out was due to you drinking energy drinks with alcohol?	Not at all Somewhat Mostly All

2. Below are a number of side-effects that people may experience while drinking energy drinks with alcohol (either mixed together in the one drink or drunk as separate drinks in the one drinking session). Please indicate how frequently you have experienced these side-effects in the ***last 6 months* while:** **1. Drinking alcohol only** **2. Drinking energy drinks with alcohol**					
Headaches					
While drinking alcohol only	Never	Less than half the time	Half the time	More than half the time	All the time
While drinking energy drinks with alcohol	Never	Less than half the time	Half the time	More than half the time	All the time
Heart palpitations (e.g., irregular, unusually slow, or unusually fast heartbeat)					
While drinking alcohol only	Never	Less than half the time	Half the time	More than half the time	All the time
While drinking energy drinks with alcohol	Never	Less than half the time	Half the time	More than half the time	All the time
Dizziness (e.g., feeling unsteady, lightheaded, or giddy)					
While drinking alcohol only	Never	Less than half the time	Half the time	More than half the time	All the time
While drinking energy drinks with alcohol	Never	Less than half the time	Half the time	More than half the time	All the time
Tremors (e.g., shaking or trembling)					
While drinking alcohol only	Never	Less than half the time	Half the time	More than half the time	All the time
While drinking energy drinks with alcohol	Never	Less than half the time	Half the time	More than half the time	All the time
Nausea (e.g., feeling of sickness)					
While drinking alcohol only	Never	Less than half the time	Half the time	More than half the time	All the time
While drinking energy drinks with alcohol	Never	Less than half the time	Half the time	More than half the time	All the time

Vomiting					
While drinking alcohol only	Never	Less than half the time	Half the time	More than half the time	All the time
While drinking energy drinks with alcohol	Never	Less than half the time	Half the time	More than half the time	All the time
Increase in saliva					
While drinking alcohol only	Never	Less than half the time	Half the time	More than half the time	All the time
While drinking energy drinks with alcohol	Never	Less than half the time	Half the time	More than half the time	All the time
Increased sweating					
While drinking alcohol only	Never	Less than half the time	Half the time	More than half the time	All the time
While drinking energy drinks with alcohol	Never	Less than half the time	Half the time	More than half the time	All the time
Vision difficulties (e.g., blurry sight)					
While drinking alcohol only	Never	Less than half the time	Half the time	More than half the time	All the time
While drinking energy drinks with alcohol	Never	Less than half the time	Half the time	More than half the time	All the time
Difficulty breathing (e.g., wheezing, feeling short of breath)					
While drinking alcohol only	Never	Less than half the time	Half the time	More than half the time	All the time
While drinking energy drinks with alcohol	Never	Less than half the time	Half the time	More than half the time	All the time
Difficulty walking (e.g., stumbling, inability to walk straight)					
While drinking alcohol only	Never	Less than half the time	Half the time	More than half the time	All the time
While drinking energy drinks with alcohol	Never	Less than half the time	Half the time	More than half the time	All the time

Jolt and crash episodes (increased energy and alertness followed by a sudden drop in energy)					
While drinking alcohol only	Never	Less than half the time	Half the time	More than half the time	All the time
While drinking energy drinks with alcohol	Never	Less than half the time	Half the time	More than half the time	All the time
Agitation (e.g., increased fidgeting, wriggling)					
While drinking alcohol only	Never	Less than half the time	Half the time	More than half the time	All the time
While drinking energy drinks with alcohol	Never	Less than half the time	Half the time	More than half the time	All the time
Hearing disturbance (e.g., ringing ears)					
While drinking alcohol only	Never	Less than half the time	Half the time	More than half the time	All the time
While drinking energy drinks with alcohol	Never	Less than half the time	Half the time	More than half the time	All the time
Slurred or slowed speech					
While drinking alcohol only	Never	Less than half the time	Half the time	More than half the time	All the time
While drinking energy drinks with alcohol	Never	Less than half the time	Half the time	More than half the time	All the time
Increased speed of speech (e.g., talking faster than normal)					
While drinking alcohol only	Never	Less than half the time	Half the time	More than half the time	All the time
While drinking energy drinks with alcohol	Never	Less than half the time	Half the time	More than half the time	All the time
Inability to sleep					
While drinking alcohol only	Never	Less than half the time	Half the time	More than half the time	All the time
While drinking energy drinks with alcohol	Never	Less than half the time	Half the time	More than half the time	All the time

3. Below are a number of moods that people may experience while drinking alcohol and energy drinks together (either mixed together in the one drink or drunk as separate drinks in the one drinking session). Please indicate how frequently you experienced these moods in the *last 6 months* while:

1. **Drinking alcohol only**
2. **Drinking energy drinks with alcohol**

I felt alert					
While drinking alcohol only	Never	Less than half the time	Half the time	More than half the time	All the time
While drinking energy drinks with alcohol	Never	Less than half the time	Half the time	More than half the time	All the time
I felt confused					
While drinking alcohol only	Never	Less than half the time	Half the time	More than half the time	All the time
While drinking energy drinks with alcohol	Never	Less than half the time	Half the time	More than half the time	All the time
I felt calm					
While drinking alcohol only	Never	Less than half the time	Half the time	More than half the time	All the time
While drinking energy drinks with alcohol	Never	Less than half the time	Half the time	More than half the time	All the time
I felt exhausted					
While drinking alcohol only	Never	Less than half the time	Half the time	More than half the time	All the time
While drinking energy drinks with alcohol	Never	Less than half the time	Half the time	More than half the time	All the time
I felt energetic					
While drinking alcohol only	Never	Less than half the time	Half the time	More than half the time	All the time
While drinking energy drinks with alcohol	Never	Less than half the time	Half the time	More than half the time	All the time

I felt annoyed					
While drinking alcohol only	Never	Less than half the time	Half the time	More than half the time	All the time
While drinking energy drinks with alcohol	Never	Less than half the time	Half the time	More than half the time	All the time
I felt stimulated					
While drinking alcohol only	Never	Less than half the time	Half the time	More than half the time	All the time
While drinking energy drinks with alcohol	Never	Less than half the time	Half the time	More than half the time	All the time
I felt aggressive					
While drinking alcohol only	Never	Less than half the time	Half the time	More than half the time	All the time
While drinking energy drinks with alcohol	Never	Less than half the time	Half the time	More than half the time	All the time
I felt outgoing					
While drinking alcohol only	Never	Less than half the time	Half the time	More than half the time	All the time
While drinking energy drinks with alcohol	Never	Less than half the time	Half the time	More than half the time	All the time
I felt active					
While drinking alcohol only	Never	Less than half the time	Half the time	More than half the time	All the time
While drinking energy drinks with alcohol	Never	Less than half the time	Half the time	More than half the time	All the time
I felt carefree					
While drinking alcohol only	Never	Less than half the time	Half the time	More than half the time	All the time
While drinking energy drinks with alcohol	Never	Less than half the time	Half the time	More than half the time	All the time

I felt daring					
While drinking alcohol only	Never	Less than half the time	Half the time	More than half the time	All the time
While drinking energy drinks with alcohol	Never	Less than half the time	Half the time	More than half the time	All the time
I felt friendly					
While drinking alcohol only	Never	Less than half the time	Half the time	More than half the time	All the time
While drinking energy drinks with alcohol	Never	Less than half the time	Half the time	More than half the time	All the time
I felt adventuresome					
While drinking alcohol only	Never	Less than half the time	Half the time	More than half the time	All the time
While drinking energy drinks with alcohol	Never	Less than half the time	Half the time	More than half the time	All the time
I felt sociable					
While drinking alcohol only	Never	Less than half the time	Half the time	More than half the time	All the time
While drinking energy drinks with alcohol	Never	Less than half the time	Half the time	More than half the time	All the time
I felt headstrong					
While drinking alcohol only	Never	Less than half the time	Half the time	More than half the time	All the time
While drinking energy drinks with alcohol	Never	Less than half the time	Half the time	More than half the time	All the time
I felt sad					
While drinking alcohol only	Never	Less than half the time	Half the time	More than half the time	All the time
While drinking energy drinks with alcohol	Never	Less than half the time	Half the time	More than half the time	All the time

I felt on edge					
While drinking alcohol only	Never	Less than half the time	Half the time	More than half the time	All the time
While drinking energy drinks with alcohol	Never	Less than half the time	Half the time	More than half the time	All the time
I felt impulsive					
While drinking alcohol only	Never	Less than half the time	Half the time	More than half the time	All the time
While drinking energy drinks with alcohol	Never	Less than half the time	Half the time	More than half the time	All the time
I felt disinhibited (e.g., felt able to say/do things wouldn't say/do normally)					
While drinking alcohol only	Never	Less than half the time	Half the time	More than half the time	All the time
While drinking energy drinks with alcohol	Never	Less than half the time	Half the time	More than half the time	All the time
I felt irritable					
While drinking alcohol only	Never	Less than half the time	Half the time	More than half the time	All the time
While drinking energy drinks with alcohol	Never	Less than half the time	Half the time	More than half the time	All the time

In the last 6 months, did you reduce the amount of energy drink(s) you had with alcohol or stop drinking energy drinks with alcohol?

Yes 1
No ..... 2 *(Skip to Section E)*

If yes, what were your motivations for reducing the amount of energy drink(s) you had with alcohol or for no longer drinking energy drinks with alcohol? *(Mark all relevant responses)*

Didn't like the taste anymore 1
Too expensive 2
Didn't like the side-effects while intoxicated 3
Didn't like the side-effects while recovering from use 4
Other ..... 5 **Specify**_____

1. **In the last 6 months, how frequently did you smoke a cigarette? *(Mark one response)***

Never 0
Monthly 1
Fortnightly 2
Weekly 3
Daily 4

2. **From the time you woke up to the time you went to sleep yesterday, how many times did you eat/drink the following caffeine-containing products: (e.g., I drank two cups of tea = 2)**

_____ Instant coffee (250mL)

_____ Ground coffee (250mL)

_____ Decaffeinated coffee (250mL)

_____ Tea (250mL)

_____ Hot/cold chocolate drink (250mL)

_____ Can of soft drink (300mL)

_____ Bottle of soft drink (600mL)

_____ Small chocolate bar (20g; e.g., standard Mars Bar)

_____ Large chocolate bar (50g-80g; e.g., king size Mars Bar)

_____ Sports drink (e.g., Powerade)

_____ Energy drink (250mL; e.g., Red Bull)

_____ No Doz tablet

_____ Other caffeine-containing product (**Specify**_____)

3. **In the past 6 months have you taken any drugs which are illegal, such as cannabis, ecstasy, cocaine, and/or speed? *Please remember all information will be kept confidential.***

Yes 1
No ..... 2 *(Skip to Section F)*

4. **Which illegal drugs have you taken in the past 6 months? (*Mark all relevant responses)***

Cannabis (weed, pot) 1
Ecstasy 2
Methamphetamine (speed) 3
Cocaine 4
Other ..... 5 **Specify**_____

1. **What is your gender? *(Please circle)***

   Female 0
   Male 1
   Transgender 2

2. **What is your current age in years?**

   _____ years

3. **What is your current residential postcode?**

   _____ postcode

4. **What is the highest year of primary or secondary school you have completed? *(Mark one response)***

   Did not go to school 1
   Year 8 or below 2
   Year 9 or equivalent 3
   Year 10 or equivalent 4
   Completed HSC/HEC (Year 12 or equivalent) 5

5. **Have you completed any further educational qualifications? *(Mark one response)***

   No ..... 0 *(Skip to Q7)*
   No, still studying for first qualification ..... 1 *(Go toQ6)*
   Yes ..... 2*(Skip to Q7)*

6. **What qualification/s are you currently studying for? *(Mark all that apply)***

   Trade Certificate 1
   Other Certificate (e.g., TAFE, Cert III) 2
   Associate or Undergraduate Diploma 3
   Bachelor's Degree 4
   Graduate Diploma/Certificate 5
   Honours Degree 6
   Postgraduate Degree 7
   Other ..... 8 **Specify** _____

7. What is the highest level of further education you have so far reached? *(Mark one response)*

Trade Certificate 1
Other Certificate (e.g., TAFE, Cert III) 2
Associate or Undergraduate Diploma 3
Bachelor's Degree 4
Graduate Diploma/Certificate 5
Honours Degree 6
Postgraduate Degree 7
Other ..... 8 **Specify**_____

8. How would you best describe your current employment situation? *(Mark one response)*

Not employed 1
Retired/pensioner 2
Home duties 3
Part time/causal work (20 or less hours per week) 4
Full time work 5
Other ..... 6 **Specify**_____

1. Below are some statements which describe different ways people think and act. For each item, indicate how much you agree or disagree with what the item says. Please be as accurate and honest as you can be. Respond to each item as if it were the only item. That is, don't worry about being "consistent" in your responses.

	Very true for me	Somewhat true for me	Somewhat false for me	Very false for me
When I want something I usually go all-out to get it.	O	O	O	O
When I go after something I use a "no holds barred" approach.	O	O	O	O
When I get something I want, I feel excited and energized.	O	O	O	O
It would excite me to win a contest.	O	O	O	O
I go out of my way to get things I want.	O	O	O	O
When I'm doing well at something I love to keep at it.	O	O	O	O
When I see an opportunity for something I like I get excited right away.	O	O	O	O
If I see a chance to get something I want I move on it right away.	O	O	O	O
When good things happen to me, it affects me strongly.	O	O	O	O

2. Below are some more statements that describe ways in which people act and think. For each statement, please indicate how much you agree or disagree. There are no right or wrong answers, and no trick questions. Do not think for too long about the exact meaning of the question.

	Yes	No
Do you often get into a jam because you do things without thinking?	O	O
Do you get so 'carried away' by new and exciting ideas that you never think of possible snags?	O	O
Do you think an evening out is more successful if it is unplanned or arranged at the last moment?	O	O
Before making up your mind, do you consider all the advantages and disadvantages?	O	O
Do you often do things on the spur of the moment?	O	O
Do you prefer to 'sleep on it' before making decisions?	O	O
Do you mostly speak without thinking things out?	O	O
Do you often buy things on impulse?	O	O
Do you usually make up your mind quickly?	O	O
When people shout at you, do you shout back?	O	O
Do you often get involved in things you later wish you could get out of?	O	O
Would you agree that almost everything enjoyable is illegal or immoral?	O	O
Are you an impulsive person?	O	O
Do you generally do and say things without stopping to think?	O	O
Do you usually work quickly, without bothering to check?	O	O
Are you often surprised at people's reactions to what you do or say?	O	O
Do you usually think carefully before doing anything?	O	O
Do you need to use a lot of self-control to keep out of trouble?	O	O
Do you often change your interests?	O	O

3. Below are some more statements that describe ways in which people act and think. For each statement, please indicate how much you agree or disagree. While some statements may seem repetitive, please provide a careful and accurate response for each statement.

	True	False
I am good at careful reasoning.	O	O
I enjoy working out problems slowly and carefully.	O	O
I often make up my mind without taking the time to consider the situation from all angles.	O	O
I often get into trouble because I don't think before I act.	O	O
Before making any important decision, I carefully weigh the pros and cons.	O	O
Often, I don't spend enough time thinking over a situation before I act.	O	O
Many times the plans I make don't work out because I haven't gone over them carefully enough in advance.	O	O
I often say and do things without considering the consequences.	O	O
I will often say what comes into my head without thinking first.	O	O
I frequently make appointments without thinking about whether I will be able to keep them.	O	O
I rarely get involved in projects without first considering the potential problems.	O	O
I frequently buy things without thinking about whether or not I can really afford them.	O	O

Thank you for your time and effort in completing this survey!

Research Participation:

Research is only possible due to the generous nature of those who volunteer to participate. As researchers, we are constantly indebted to those who give up their time and resources to participate.

If you are interested in participating in further research on energy drink and alcohol consumption, and you live in the greater Hobart area, please click on the link below and you will be redirected to a secure webpage where you can enter your contact details.

Prize Draw:

To thank you for your participation, you have the opportunity to enter a prize draw to win an Apple IPad.

To enter the prize draw, please click on the link below and you will be redirected to the secure prize draw entry webpage where you can enter your contact details.

Please note that each participant can only complete the survey once, and can only enter the prize draw once. If you do not select the link below you will be unable to enter the prize draw.

KHA111/112 Research Participation:

KHA111/112 students can lodge their request for research participation credit by clicking on the link below and entering their student number and campus of study. Please note that you cannot enter the prize draw if you are claiming research participation credit.

Link: https://surveys.psychol.utas.edu.au/index.php?sid=31444&lang=en

Questions and Comments:

Please feel free to contact us on the following details with any comments or queries regarding this survey:

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Appendix D: Valid Points but the Trends Remain: A Response to Rossheim, Suzuki, and Thombs

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Peacock, A., Bruno, R., & Martin, F. (2013). Valid points but the trends remain: A response to Rossheim, Suzuki, and Thombs. *Alcoholism: Clinical and Experimental Research, 37,* 2171-2174.

B.1 Preface

The following manuscript comprises the Candidate's response to a Letter to the Editor published by Rossheim et al. (2013) in regards to the manuscript in *Chapter 4*. This manuscript addresses those concerns raised by Rossheim et al. (2013) and confirms that the findings reported in the original publication are reflected in subsequent analyses.

B.2 Letter to the Editor

Rossheim et al. (2013) detail in a Letter to the Editor their concerns regarding our recent publication "The Subjective Physiological, Psychological, and Behavioral Risk-Taking Consequences of Alcohol and Energy Drink Co-Ingestion" (Peacock et al., 2012). Specifically, the authors outline several issues with the study design and analyses, particularly the failure to account for the relative frequency of alcohol versus alcohol mixed with energy drink (AmED) drinking sessions when determining the odds of risk behaviour according to session type. While we acknowledge the validity of many of the points raised by Rossheim et al. (2013), re-analysis of the data demonstrates that it is not likely that these issues have substantially affected the findings.

The first issue raised in the letter concerns the proposed length of the survey. Rossheim et al. (2013) argue that based on the 10 to 30 minute survey containing 303 items, participants would have responded to each item in between 2 and 6 seconds. However, as it is noted in the original manuscript, survey completion time was dependent on participants' history of alcohol and energy drink (ED) use, as the AmED user subsample (n=403) on which the original manuscript was based was selected from a broader sample (N=1113) invited to partake in the study regardless of whether they had consumed alcohol or EDs independently or in combination Thus, the use of survey logic meant that participants only completed select relevant items and Rossheim and colleagues' calculations present a misrepresentation of the response time. Rossheim et al. (2013) further assert that "given such quick responses to a relatively long survey, questions need to be raised about whether participants responded indiscriminately to survey items merely for a chance to win an Apple

iPad2®" (p. 2). However, several validity checks included in the survey demonstrate the high consistency of responses. For example, only five of 403 AmED consumers reported their frequency of AmED consumption in the last six months as 'never' despite answering in the affirmative to an earlier dichotomous choice item assessing whether they had consumed an AmED in the last six months. This, and the multiple other logic checks within the survey, meant that it was unlikely that participants were responding indiscriminately. We should note that the use of a lottery material incentive system is common and recommended in survey research to increase response rates (Goritz, 2006). In our survey, prize draw entry was dependent on the submission of the survey rather than requiring completion of all items, thus reducing the likelihood of participants replying randomly simply to ensure entry. Moreover, less than three-quarters (71%) of participants went on to enter their contact details for the prize draw – clearly demonstrating that the potential for the prize was not coercing the rapid or inaccurate completion of responses.

The second issue raised in the letter refers to the validity of response items which asked participants to attribute their involvement in risk behaviour to AmED consumption. We would argue that these results do contribute to the science on caffeinated alcohol consumption. It has been routine for participants in experimental AmED research to rate their subjective physiological, psychological, and behavioural state of intoxication as a consequence of treatment administration (Ferreira et al., 2006; Marczinski et al., 2011; Marczinski et al., 2012). Just as we frequently ask consumers to rate their expectancies regarding the effects of caffeinated alcohol consumption (MacKillop et al., 2012) , we included this question only to determine consumer perception of the effects based on their recent

experiences of AmED. The accuracy of their perception is not directly relevant, as we did not attempt to use these results to infer whether there was a direct pharmacological effect of AmED on risk-taking behaviour. Rather, these results were only ever presented as a secondary outcome, to indicate consumer perception of the association between AmED consumption and risk-taking.

The primary issue raised in the letter concerns the frequency of AmED versus alcohol drinking sessions in the calculation of odds ratios regarding the likelihood of risk-taking according to session type. We stated in the original publication that AmED was typically ingested on a monthly or less basis while alcohol was consumed on a fortnightly to thrice weekly basis. Rossheim et al. (2013) have consequently argued that there would be more opportunities for risk behaviours due to the greater number of alcohol sessions in the period of interest. This is a reasonable conclusion. We concur that analyses taking into account the respective frequency of each session type would provide a more accurate indication of the associated risks. However, this cannot be achieved with the data from the current study. To determine the impact of this limitation, we selected a subsample of participants who had an equal frequency of alcohol and AmED sessions. This comprised 74 individuals, 54% (*n*=40) who ingested alcohol and AmED on a less than monthly basis, 41% (*n*=30) who ingested alcohol and AmED 2 to 4 times a month, and 5% (*n*=4) who ingested alcohol and AmED two to three times a week. Despite the lower power, the initially reported effects were apparent in relation to 21 of the 26 risk behaviours under study: namely, the percentage of consumers engaging in each risk behaviour was higher in alcohol than in occasions of AmED consumption (Table 1). The remaining five behaviours were equally present in both

session types or practically so (within 1-2%). Thus, despite the limitations of the initial analysis, this re-analysis suggests that the actual impact on the findings was minimal: the data generally support the original analyses demonstrating that the frequency of engaging in risk-taking behaviour was lower in AmED compared to alcohol drinking sessions.

The final issue raised by Rossheim et al. (2013) relates to the reporting of physiological and psychological side-effects of AmED and alcohol consumption. We acknowledge Rossheim et al. (2013) raise valid points in regards to potential biases through the use of qualitative categories (i.e., 'never', 'less than half the time', 'half the time', 'more than half the time', and 'all the time') to determine side-effect frequency in AmED and alcohol drinking sessions. Consequently, we re-analysed the data so that *any* experience of the side-effect ('less than half the time', 'half the time', 'more than half the time', and 'all the time') resulted in classification of the symptom as present. We restricted our analyses to: (i) the subsample with matched frequency of AmED and alcohol sessions (n=74) and (ii) physiological outcomes only, being of greater relevance than the psychological outcomes from a healthcare perspective. Again, all but one of the physiological outcomes matched the reports from the original manuscript: more consumers reported experiencing heart palpitations, tremors, jolt and crash episodes, increased speed of speech, and sleep difficulties and fewer consumers reported experiencing nausea, vision and walking difficulties, and slurred speech, in AmED versus alcohol sessions (Table 1). The only outcome which did not reflect the original analyses with the smaller matched subsample was 'agitation', which had a similar, but slightly lower, frequency in AmED relative to alcohol sessions.

In sum, despite the valid issues raised by Rossheim et al. (2013), the direction of the effects identified in the original article remain in a sample with equal frequency of alcohol and AmED drinking sessions: risk-taking and sedating side effects of alcohol appear less commonly; and stimulatory side effects appear more commonly; in AmED drinking sessions compared with consuming alcohol alone.

As noted in the original manuscript, there is a paucity of research involving within-subject comparison of risk-taking in AmED and alcohol drinking sessions. Those studies involving cross-sectional comparison of risk-taking by AmED consumers versus alcohol consumers strengthen our knowledge base as they offer insight into the characteristics of the two consumer types (e.g., O'Brien et al., 2008). Similarly, those studies which compare consumers' expectancies of behavioural outcomes in AmED versus alcohol drinking sessions elucidate consumers' perceptions of the effects of AmED (e.g., Woolsey et al., 2010). However, these studies also have methodological weaknesses, in that they cannot tell us about the direct pharmacological effect of AmED on risk-taking. In the former case, risk-taking behaviour is typically reported for all alcohol drinking sessions as opposed to AmED versus alcohol specific-risk-taking. Furthermore, higher rates of risk-taking may be an outcome of systematic individual differences between consumers (e.g., trait impulsivity; Brache & Stockwell, 2011) rather than a direct consequence of beverage ingestion. In the latter case, consumers are reporting on an expectation or an intention which may not necessarily translate into actual risk-taking behaviour.

Table 1

Percentage of Consumers Reporting Risk Behaviours in AmED and Alcohol Drinking Sessions for the: (i) Overall AmED Sample (N=403) Reported in Peacock, Bruno, and Martin (2013) and (ii) Subsample of AmED Consumers With Matched Frequency of AmED and Alcohol Drinking Sessions (n=74)

Outcome	**Overall AmED Consumer Sample (*N*=403)**		**Matched Drinking Session Frequency AmED Consumer Subsample (*n*=74)**	
	Alcohol Session (%)	**AmED Session (%)**	**Alcohol Session (%)**	**AmED Session (%)**
Behavioural Outcomes:				
Smoked cigarettes	45	32	49	41
Drank more alcohol than planned	75	62	64	59
Used legal drugs for recreational purposes *	14	8	4	4
Used illegal drugs	29	15	18	15
Had sex with someone recently met	33	19	25	15
Did not use contraception	27	16	25.	19
Was touched in unwanted sexual way	15	7	14	10
Touched someone in unwanted sexual way *	6	3	3	3
Drove while over legal alcohol limit	15	4	11	4
Passenger while driver over the legal alcohol limit	20	5	14	7
Seatbelt omission *	9	4	5	5
In vehicle with illegal passenger number	25	10	23	16
In vehicle exceeding speed limit by at least 10%	8	5	8	5
Spent more money than planned +	75	59	58	60
Gambled	24	10	23	18
Verbally fought	32	16	34	24
Physically fought	14	8	16	11
Acted in way that resulted in guilt	49	26	34	20

Table 1 Continued

Outcome	Overall AmED Consumer Sample (*N*=403)		Matched Drinking Session Frequency AmED Consumer Subsample (*n*=74)	
	Alcohol Session (%)	AmED Session (%)	Alcohol Session (%)	AmED Session (%)
Behavioural Outcomes Continued:				
Acted in a way that resulted in humiliation	46	30	35	25
Passed out	32	18	20	16
Physically hurt or injured	27	14	21	13
Required medical treatment	3	1	3	1
Acted on a dare which could cause harm	15	9	14	8
Asked to leave drinking establishment	21	11	14	4
Vandalised +	5	2	1	3
Cautioned/charged by police	4	2	6	4
Physiological Outcomes:				
Heart palpitation	6	27	25	45
Tremors	10	22	27	28
Nausea	32	28	77	68
Vision difficulty	20	17	51	49
Difficulty walking	34	29	78	69
Jolt and crash episode	15	22	42	45
Agitation -	10	19	40	38
Slurred speech	31	24	69	59
Increased speed of speech	21	26	46	47
Inability to sleep	11	34	41	53

Note. Only those behavioural and physiological outcomes which had significantly higher/lower odds in alcohol versus AmED sessions in the original manuscript are displayed here. The percentages for the physiological outcomes represent those consumers who reported the outcome as occurring 'less than half the time', 'half the time', 'most of the time' and 'all the time' for the session type. Items are identified which show differing results for the 'matched drinking session frequency AmED consumer group' relative to the original full AmED consumer subsample (reported in . These items are identified according to whether the 'matched drinking session frequency AmED group' display either lower frequency (-), equivalent frequency (*), or greater frequency (+) in the AmED relative to alcohol drinking sessions.

We undertook our survey as a first step towards rectifying this situation and, like all research; it has methodological strengths and weaknesses. We concur with Rossheim et al. (2013) that further work is required to understand the relationship between AmED consumption and risk-taking behaviour; we would by no means treat our study as a definitive statement and it would be ambitious to think that the results of our single study will bring about "policies that fail to protect public health" (Rossheim et al., 2013, p. 9). This was the first study to undertake a within-subject comparison of risk-taking according to session type; further studies with general population and high-risk university student samples utilising a similar within-subject design are necessary. While logistically challenging, these studies could use prospective data to overcome the limitations of retrospective recall outlined above. Additionally, as suggested in the original manuscript, future research undertaking within-subject comparison of objective risk-taking via laboratory-based instruments would directly determine the pharmacological effect of AmED relative to alcohol on risk-taking. Conclusions drawn from such research will still be beset with limitations due to reduced ecological validity but would rule out any biases of self-report.

Until such research is conducted, we cannot make a definitive conclusion regarding the additional harms of AmED on risk-taking. Some reviewers might be inclined to consider this absence of definitiveness as an unsurmountable flaw of the current study, however, we would argue to the contrary, taking into consideration the context of a current lack of research on this topic, and the fact that the original outcomes still hold true when we undertake analyses to address the valid points raised by Rossheim et al. (2013). We would hope that our research, and that of those before us, can serve as a starting point to refine the methodology of these future

studies, so as to strengthen the evidence base which can be used to inform policy change regarding AmED sales and regulation to protect public health.

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