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Mixing alcohol and energy drinks: Acute subjective effects in a double-blinded randomized controlled trial.

Degree project in medicine

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C O N T E N T

Abstract

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BACKGROUND

The mix of alcohol and energy drinks has been linked to various mental and physical problems, such as underestimation of degree of alcohol intoxication, alcohol addiction, risk taking behavior and physical injury. Students report that they combine energy drink with alcohol to mask the sedating effects of alcohol. Complete understanding about the effects of the mix are still to be explained and one way to approach this question could be to investigate the acute subjective effects in a controlled environment.

AIM

We wanted to investigate whether we could find any details in the subjective effects that might provide a clue to some of the observed behavioral effects of alcohol mixed with energy drinks using the Biphasic alcohol effects scale (BAES) and the Profile of mood states (POMS), two instruments designed to measure different subjective states.

MATERIALS AND METHODS

This study was conducted as a double-blind randomized controlled trial. A total of 61 subjects were randomized to one of the following four treatments; 1. Placebo, 2. Energy drink, 3. Placebo + alcohol, 4. Energy drink + alcohol. To investigate the subjective effects of alcohol and energy drinks, we used BAES and POMS, two widely used questionnaires designed to measure different aspects of subjective mood states. Both questionnaires were completed three times each to look for any differences between the treatment groups; at baseline before consumption, at 20 minutes and at 60 minutes.

RESULTS

A significantly higher score for alcohol compared to placebo was revealed on BAES ‘stimulation’ at 20 minutes and on POMS ‘confusion’ at 60 minutes. A significantly higher score for alcohol compared to placebo was revealed on BAES ‘sedation’ both at 20 and 60 minutes. No measurements were significant for energy drink alone. A higher score with a significant interaction effect between alcohol and energy drink was revealed for BAES ‘sedation’ at 60 minutes.

DISCUSSION AND CONCLUSIONS

As expected BAES was able to measure the stimulative and sedative effects of alcohol. POMS was only significant on ‘confusion’ and we conclude that POMS bring no additional information over BAES when measuring the acute effects of alcohol or energy drink. No measurements were significant for energy drink alone and under our experimental conditions it is questionable whether energy drink has any subjective effects at all. An interaction effect of the mix was revealed on BAES ‘sedation’ where subjects who received the mix reported higher score on this item. This result stand in contradiction to the reason why students drink the mix and we speculate that there is a discrepancy of how individuals report the mood-altering effects of the mix depending on when they report it. The result could explain how individuals underestimate the level of intoxication, which in turn might lead to an increased intake of alcohol and in the end a high-risk behavior. With this knowledge, it is important for people who consume alcohol in combination with energy drink to be aware of the plausible risk of the combination and that the effects are not certainly what the drinker often expects.

KEY WORDS

Energy drink, Alcohol, Subjective effects, Profile of mood states, Biphasic alcohol effects scale

Abbreviations

AL	Ascending limb of blood alcohol concentration
AmED	Alcohol mixed with energy drink
AUDIT	Alcohol use disorders identification test
BAC	Blood alcohol concentration
BAES	Biphasic alcohol effects scale
BAL	Breath alcohol level
BRS	Brain reward system
CANTAB	Cambridge neuropsychological test automated battery
DALY	Disability-adjusted life years
DL	Descending limb of blood alcohol concentration
ED	Energy drink
GABA	Gamma-aminobutyric acid
NAc	Nucleus accumbens
POMS	Profile of mood states
SCL-90	Symptom checklist 90
TMD	Total mood disturbance
VTA	Ventral tegmental area
WHO	World health organization

Background

Energy drinks

Since the introduction in the 1980's, energy drinks (EDs) have increased exponentially in popularity for the most part among adolescents and young individuals [1]. During 2014 EDs sold for an estimated 50 billion dollars all over the world and sales are estimated to increase with an annual rate of 3.5% until the year of 2020 [2]. Due to its linkage to drug abuse, alcohol abuse, and cardiovascular disease, EDs have become a commonly debated subject [3-8]. Many are concerned about what effects high consumption of EDs may have both in the long and in the short term. Questions and concerns have been raised from medical professionals, researchers, parents and politicians and some countries have already legislated minimum age requirements for purchasing these products [9-11]. EDs often marketed as mind and body enhancing with the ability to increase mood, endurance, performance, concentration, alertness. Surveys have also mapped that students often use them to compensate for lack of sleep [1, 6, 11, 12]. EDs contain high concentrations of centrally active caffeine and taurine. Other common ingredients are sugar, glucuronolactone, other sugars than glucose such as inositol, vitamins, and other amino acids [13]. Both taurine and caffeine will be discussed more thoroughly further down in this thesis. Glucuronolactone is a molecule that can be synthesized by our cells and is found in high concentrations in connective tissue. It is also known that the molecule is used by the liver to conjugate metabolites and toxic substances, thus making them water soluble and allowing for these waste products to leave the body via diuresis. This fact has been used by many companies who claim that their drinks have "detoxifying abilities". However, dietary intake of glucuronolactone has not been proven to increase this process by the liver [14].

Taurine

Taurine is a molecule derived from the amino acid cysteine. It is synthesized in the liver but can also be acquired through diet, where fish and meat are some of the common high-containing sources [15]. Animal studies have shown that complete depletion leads to a variety of different pathological conditions including cardiomyopathy, immunologic dysfunction, kidney dysfunction and retinal disease [16-19]. Our bodies contain taurine in a concentration of about 1g/kg body weight. In the literature, taurine is often mentioned as an amino acid. However, in strict biochemical terms this is not entirely true since it has a sulfonic group instead of a carboxyl group. Nevertheless, taurine is an essential molecule important to both fetal development and in adults. It has effects in skeletal muscle tissue, in the central nervous system (CNS) and in many other tissues. More specifically taurine has been shown to be involved processes like the control of calcium channels, cell membrane stabilization, osmotic regulation, conjugation of bile acids, as an antioxidant, and more recent as a signaling molecule in our brain [15, 20]. Taurine passes over the blood-brain barrier through sodium- and chloride dependent channels, various other active transporter proteins, and possibly osmosis [21, 22]. Also, ischemic injury has been shown to increase the transport from blood to the brain [23]. Much is known about the role of taurine in peripheral parts of the body, but little is understood about its CNS function. It seems that taurine is involved in both general and more specific processes in our brain. One of the mechanism, relevant for this thesis, by which taurine exerts its function in the CNS is the binding to the glycine receptors in the nucleus accumbens (NAc), an essential structure in the brain reward system (BRS). Studies have shown that taurine is involved in mediating the acute effects of alcohol in the BRS and thereby possibly involved in the development of alcohol addiction [24, 25]. Animal studies have shown that taurine can exert signal-inhibiting capabilities between neurons, for example the ability to prevent epileptic seizure. Taurine is also involved in the process of long-term

potentiation, which is a type of modulatory activity that strengthens synaptic signaling between neurons [26, 27]. More studies are needed to further understand the diverse role of taurine in the CNS.

Caffeine

The alkaloid caffeine is a psychoactive substance used by coffee-drinkers all over the world. Humans have consumed coffee since the 15th century and possibly even earlier than that. Other common sources of caffeine are tea leaves and soft drinks. Caffeine in high doses has been shown to increase anxiety and tension. Using caffeine in a stressful situation has been shown to increase the anxiogenic effect of caffeine to an even greater extent [28]. Caffeine can reduce fatigue, increase performance and vigilance, and increase reaction time [29, 30]. Caffeine can act as an antagonist to the adenosine receptor. Adenosine is a purine nucleoside neurotransmitter which has inhibitory effects in the CNS leading to increased sedation and tiredness. By blocking this receptor caffeine increases alertness. Caffeine also increases the activity in the BRS and might have a role in the development of addiction [30-32]. A daily intake of 400 mg for adults, 300 mg for healthy pregnant women, and 2.5 mg per kg body weight for children and adolescents is generally considered safe. However, for children and adolescents this information is based on very limited data [33]. EDs vary in their concentration of caffeine, from 50 mg up to 505 mg per bottle. Hence, for children and adolescents the risk of consumption far above today's recommendations is apparent when consuming EDs [11].

Alcohol

The term ‘alcohol’ is defined as an organic compound having a hydroxyl group (-OH) bound to one of its carbon atoms. Here, the term alcohol will be used for of ethanol, an alcohol molecule that consists of two carbon atoms with one having a hydroxyl group bound to it. In nature, yeast produce ethanol as a by-product in its metabolic process. By taking advantage of this process, humans have used yeast in different ways to produce alcoholic beverages (ethanol) for thousands of years. According to a WHO-report from 2014, alcohol consumption is estimated to have caused 3.3 million deaths in 2012 worldwide (5.9% of all deaths). Also, the same year, alcohol consumption caused 139 million disability-adjusted life years (DALY) [34]. Alcohol is a small molecule with both hydrophilic and hydrophobic abilities. Because of this, alcohol can easily pass the blood brain barrier where it can bind to a variety of receptors and affect many different functions in our brain [35]. The effects of alcohol are biphasic with mood elevating effects such as feelings of euphoria and relaxation during the phase of increasing blood alcohol concentration which is also called the ascending limb (AL). This is followed by mood depressing effects such as feelings of sedation and depression during the phase of decreasing blood alcohol concentration which is also called the descending limb (DL) [36]. The mood elevating effects of alcohol in the AL are thought to be mediated by the serotonergic system (5-HT). Intake of alcohol increases the serotonergic activity and withdrawal has been shown to reduce this activity leading to opposite, mood depressing effects in the long term [37]. The acute mood depressing effects of alcohol during the DL are mainly thought to be mediated by the sedative gamma-aminobutyric acid (GABA), which is the most abundant and important inhibitory neurotransmitter in the CNS. Alcohol acts as a psychoactive drug by binding and potentiating GABA-receptors, leading to CNS-depressant effects with feelings of sedation and depression [38]. Also, alcohol has stimulatory effects in the dopaminergic brain reward system (BRS), more specifically in the nucleus

accumbens (NAc) and in the ventral tegmental area (VTA). The BRS is thought to function as a system for "incentive motivation" and compelling evidence exist that activation of the BRS is an important component in the development of addiction [39, 40]. Long-term users require higher doses of alcohol to experience the same subjective effects of alcohol. Even though alcohol affects our brain in a very complex manner, a simplified explanation of how alcohol tolerance is developed is that increased use of alcohol reduces the number of GABA-receptors. Because of this, higher concentrations of alcohol are needed to receive the same amount of stimulation. Too little stimulation leads to withdrawal symptoms [35].

Mixing alcohol and energy drinks

People who drink a mix of alcohol and energy drinks (AmED) are more likely to drink more per session than those who drink other alcoholic drinks [41]. Between 2006 and 2011, the visits in U.S. emergency departments associated with the consumption of EDs increased by ten times and half of the visits could be linked to consumption of AmEDs [42]. Even after adjusting for amounts of alcohol consumed, people who drink AmEDs have an increased risk of; physical injury, marijuana use, alcohol intoxication, not wearing a seatbelt and to ride with an intoxicated driver. AmED-consumers also have an increased risk for developing an addiction to alcohol [6, 43, 44]. A field study showed that customers at a bar who drank AmEDs had a three times increased risk of leaving the bar "highly intoxicated" compared to those that only drank alcohol [45]. Different approaches and methods have been used to further understand how the combination of these drinks affect our brain. Some studies have focused on how they affect the biochemical processes in the brain. Most studies have focused on the energy drink ingredients taurine and caffeine. Results point towards an important interplay between taurine and alcohol in the BRS of rats and that taurine is a key component in the development of alcohol addiction [24, 25]. Yet, how the combination of these drinks

affect human behavior and mood is currently unknown. A large survey-based study on college students investigated the motives for consuming these drinks and students report that they used AmED to antagonize the sedating effects of alcohol, to get drunk faster, to be able to drink more, to celebrate and to socialize [46].

Subjective measurements

To better understand more about the attractiveness of AmED and why particularly the young engage in this habit some attempts have been made to measure the subjective experience of drinking AmED in controlled conditions. Two clinical studies report that AmED-drinkers felt more stimulated than those only drinking alcohol [47, 48]. It has also been shown that during consumption, AmED-drinkers report less sleepiness compared to people who only drink alcohol. Also, in the same study AmED-drinkers felt less intoxicated at low alcohol levels [49]. Other studies report small effects or no effects at all [50, 51]. The exact mechanism of how the mix of energy drinks and alcohol affect our brain remains to be explained and one way to approach this question would be to investigate the experienced effects with broad subjective questionnaires in a controlled environment. To understand more about psychological outcomes other than stimulation and sedation which has been the focus in previous studies, it would be interesting to use an instrument that also can measure other psychological effects. An instrument suitable for this task could be the Profile of Mood States (POMS - *appendix D*) which is a neuropsychological test developed by McNair et al. created to subjectively measure transient mood changes in psychiatric outpatients [52]. POMS is generally considered a broad instrument with the ability to depict a nuanced pattern of different subjective moods and feelings. It consists of 65 statements or words that describe different moods and feelings. The subject must rate on a 5-point Likert-scale from “not at all” (0) to “extremely” (4) on how well think different feelings are experienced during the day of

testing. The questionnaire can then be retaken, after for example a specific treatment. Together these 65 statements create the 6 different clusters or subscales; ‘anger’, ‘confusion’, ’depression’, ’fatigue’, ’tension’, and ’vigor’. A commonly used term associated with POMS is the subscale ‘Total Mood Disturbance’ (TMD) which is acquired by adding the scores from the first 5 subscales, followed by the subtraction of the scores from ’vigor’. POMS has to our knowledge never been used in its original form to measure the acute subjective effects of AmED consumption. To match our results with the previous study by *Marczinski et al. 2011* who reported that AmED-drinkers felt more stimulated than alcohol drinkers, we also wanted to include the Biphasic alcohol effects scale (BAES, *appendix C*) in our study. BAES is an instrument designed to measure the acute effects of alcohol consumption and will be explained more thoroughly below.

Aim

This study was conducted to investigate different aspects of the acute subjective effects of alcohol and energy drink consumption in a controlled environment. We wanted to investigate whether we could find any details in the subjective effects that might provide a clue to some of the observed behavioral effects of AmEDs using BAES and POMS, two instruments designed to measure different subjective states.

Ethics

The study has been approved by the ethic committee of The Sahlgrenska Academy, University of Gothenburg, Sweden.

Materials and methods

Recruitment and registration

Subjects were recruited through social networks, friends, and classmates. The subjects were informed about the study in a manner that was easy to understand. They were also informed about the length of the trial (approximately 2 hours and 30 minutes). Subjects were offered two cinema tickets as compensation for participating in the study.

Screening – inclusion and exclusion

Before enrollment we screened the subjects' physical health by auscultation of their heart and lungs, and by measuring pulse and blood pressure. We also screened the subjects with different self-report questionnaires to exclude individuals with a history of psychiatric problems, history of drug-abuse, alcohol related problems, or people at risk of developing any problems of that kind. For this task we used the Swedish version of 'Symptoms checklist 90' (SCL-90, *Appendix A*) and 'Alcohol use disorders identification test' (AUDIT, *Appendix B*), plus two more questionnaires (not presented in this report) to collect information about earlier drug use and other demographic information [53, 54]. AUDIT was developed by the World Health Organization (WHO) and has been used in thousands of studies since [55]. It is a

validated instrument designed to detect people with hazardous alcohol consumption with high sensitivity and specificity [56]. The subject can score a total of 0 to 40 in this questionnaire, where 0 corresponds to low or no alcohol related problems and a score of 40 means that there are severe problems. We chose to exclude subjects with a score of more than 15 for men and more than 13 for women from the study. A score of 8-15 for men and 7-13 for women corresponds to a slight increased risk of developing alcohol related problems or that the subject already has developed such problems. In AUDIT, the recommended intervention for this group of individuals is "simple advice" about their risk-score. A score of more than 15 for men and more than 13 for women indicates that the subject has severe problems with alcohol or a consumption level at high risk. Hence, subjects with a score over 15 and 13 respectively were excluded from the study. SCL-90 is another instrument that was used to discover any psychiatric problems among subjects. It was first developed by Derogatis et al. [57] but has been revised and re-validated many times thereafter [58, 59]. Any subjects with a higher composite score (the sum of the scores on all items) of 20 or a single item score of 4 were excluded before enrollment. All women had to do a pregnancy test (Quick-Check^{TM}, Colibri Medical AB) before starting the trial in case of an unknown, planned, or ongoing pregnancy. Subjects data on alcohol drinking habits, earlier drug use, family history for alcoholism (alcoholism in the family), weight, age, and length are presented in the demographic characteristics table (Table 1 in *Tables*). A total of 3 participants were excluded after the screening. Among these two subjects were excluded due to ongoing pharmacological treatment for psychiatric problems and one due to an AUDIT score that exceeded our limit. A total of 61 participants ($N = 61$ of which 31 males and 30 females) remained after inclusion and exclusion, all of which proceeded onto the experiment. No participants aborted the study after it had started, which means that all the 61 participants fulfilled every test in the experiment.

Outcome measures

We wanted to assess whether there were any measurable subjective effects (experienced by the subject) at the time of consumption when mixing alcohol and energy drinks. In the same study, we also wanted to examine if there were any measurable objective effects from mixing alcohol with energy drinks. We did this by using the computer-based test battery 'Cambridge Neuropsychological Test Automated Battery' (CANTAB) repeatedly. We also measured blood pressure, pulse and breath alcohol level (BAL) repeatedly. However, only the subjective measures will be handled in this thesis. To study the subjective effects, we chose the widely-used questionnaires Biphasic Alcohol Effects Scale (BAES) and the original version Profile of Mood States (POMS). Both BAES and POMS were used in paper form and the tests will be discussed more thoroughly below.

Profile of mood states

Since the introduction of POMS, the instrument has been widely used in a variety of different fields and many modified versions of the tests has also been created. Many short-form versions of the test have been used, some of them entirely experimental. Among previous studies, some include selected subscales only, while some have used POMS with additional self-made subscales. This is problematic since most modified versions of POMS lack validity to their corresponding task. Other versions have been validated like the POMS-bipolar [60-62] and the short-form version POMS-adolescent [63]. The latter has also been validated for the adult population [64]. Many versions of POMS have been used in alcohol studies. However, a coherent validated version of POMS to specifically measure the acute effects of alcohol or energy drink consumption has never been presented. Nagoshi et al. has shown by using the 'Colorado Alcohol Research on Twins and Adoptees' (CARTA) procedure that some of the subscales are significantly correlated to alcohol problems in males but not in

females. A modified shortened version of POMS was used in one of their studies [65]. The results showed that only ‘confusion’ appeared to be significant in females [66]. In a small study (n=20), Robbins et al. showed that subjects had a reduction in ‘tension’ and increased ‘confusion’ with increased blood alcohol concentration (BAC). Men increased in their scores on ‘depression’ and ‘anger’ with increasing BACs [67]. De wit et al. used an experimental version of POMS with 8 subscales in two of their studies, including two non-validated subscales “on an intuitive basis” derived from the other scales. Subjects that preferred to drink alcohol over placebo in a seven-session choice procedure had higher scores on “elation” and “vigor” than placebo choosers [68]. Liguori et al. used POMS to evaluate the acute mood effects of alcohol consumption. They could not show any significant main effect on any subscale. However, the authors comment that the result might have been affected by the study design where the POMS-questionnaire was performed in the DL [69]. Howland et al. studied the effects of binge drinking in college students. They set up a double-blind randomized controlled trial by looking at the POMS subscale ‘TMD’ the day after alcohol consumption. The day after alcohol consumption the students had significantly higher score on ‘TMD’ both in the morning and in the afternoon. However, they did not perform any tests with POMS regarding the acute effects of alcohol on mood [70]. Schrieks et al. used a modified version POMS with a total of 40 items, with the addition of the two subscales ‘happiness’ and ‘calmness’, two subscales originally found in the Brunel mood scale [71, 72]. The authors claim that the “POMS subscales” ‘happiness’ increase within 1 hour after moderate alcohol consumption, while ‘calmness’ decreased. However, none of these items were included in the original POMS-questionnaire but are instead a part of the original Brunel mood scale which is a completely different instrument. Conrod et al. used the POMS-bipolar in two studies to show that alcohol-induced heart rate was positively correlated with alcohol induced mood changes in the items ‘composed-anxious’, energetic-tired’, ‘elated-depressed’, and ’confident-

unsure' [73]. Ray et al. conducted a study by looking on data from heavy drinker's BALs during alcohol administration in repeated measures. The aim was to find common subjective factors in response to alcohol usage. Here a shortened version of POMS was used with 4 subscales that could also be validated for this population. However, the external validity of this version is low, since the applicability for the general population is unknown. Also, the biphasic mood alternating effects of alcohol were not taken into consideration. Instead POMS was performed when three specific BALs with increasing concentations had been achieved [74].

To summarize the current literature about POMS; many versions, subscales, and modifications of POMS have been created and used and many of them have also been shown be able to detect mood changes in response to alcohol intake. Yet, no randomized controlled trial has been made on the original validated version of POMS to measure the acute effects of alcohol intake on the general population. The same assertion applies to the effects of energy drink consumption, and the mix of energy drink and alcohol. We therefore chose the original POMS to investigate if it can measure mood changes after consumption of these drinks alone and combined.

Biphasic alcohol effects scale

The Biphasic Alcohol Effects Scale (BAES, *Appendix C*) is a validated questionnaire developed by Martin et al. designed to objectively measure simulative and sedative subjective effects of alcohol [75]. When creating this test, the authors assessed the two subscales 'stimulation' and 'sedation', both of which consist of 7 items each. The subscale 'Stimulation' consists of items such as 'elated', 'talkative', and 'energized'. The subscale 'Sedation' consisting of items such as 'down', 'heavy head', and 'slow thoughts'. The subject has to grade on a 11-point Likert-scale ranging from "not at all" to "extremely" on how they

think every item corresponds to their current state. Later, a shorter version named Brief-BAES consisting of 6 items total was developed [76]. The shorter version was also validated and has been used in many other studies. The short-version was conducted in young heavy social drinkers and the authors conclude that this short-version of BAES has limitations when it comes to the applicability on the general population [77]. In the original validation study, BAES was performed depending on when the subject reached a specific BAL, which means that every subject filled the questionnaire at an individually set time. This is problematic since it requires a lot more resources than having a fixed set time for all participants. We therefore chose to use the original version of BAES with fixed times for this experiment at a lower dose of alcohol adjusted by the subject's weight.

Procedure and flow chart

After screening and collection of demographic data, subjects were randomized to one of the four groups. The four groups and their respective treatments were as followed: 1. Placebo (n = 14), 2. Energy drink (n = 15), 3. Placebo + alcohol (n = 16), 4. Energy drink + alcohol (n = 16). Subjects that were randomized to one of the alcohol containing groups were given Absolut Vodka® (40%), with amounts adjusted by the weight of the subject. The dose was set to 0.4 g alcohol per kg body weight, to reach an estimated BAL of 0.03-0.05%. We used Monster® Rehab Lemonade as energy drink and subjects were given 7.14 ml per kg body weight. For placebo, we used Lipton® Ice Tea Lemon, which was administered at the same volume as the energy drink. Drinks were prepared in a separate room out of sight from the experiment leader and the subject. Subjects were told by the instructor to consume the drink within 15min and not to talk about taste or effects of the drink in front of the experiment leader. BAES and POMS were performed in a repeated measure manner as follows: baseline (before drinking), at 20 minutes (during AL), and at 60 minutes (during DL).

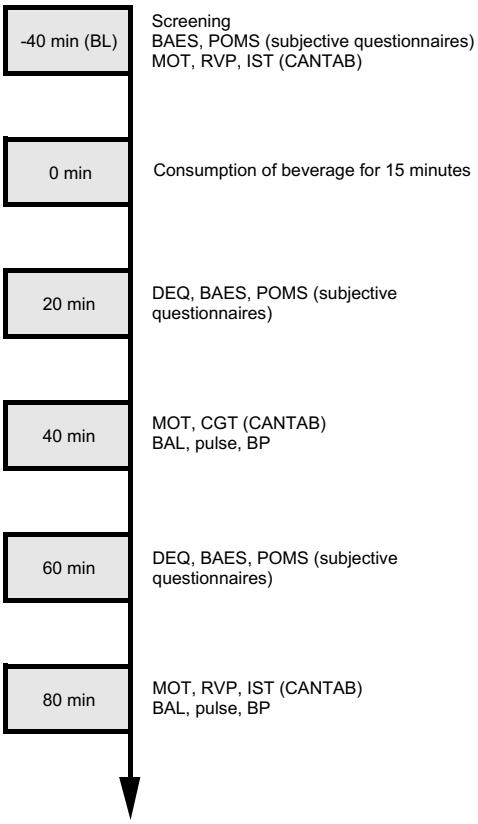

Figure A. Flow chart of the testing-procedure, displaying the order and time of all tests. Some tests were performed only once and others multiple times. For this thesis, BAES (Biphasic Alcohol Effects Scale) and POMS (Profile Of Mood States) are the tests in focus. They were all performed three times, respectively; -40 minutes (baseline), at 20 minutes, and at 60 minutes. MOT, RVP, IST, and CGT are tests within the CANTAB test-battery and will not be handled in this thesis. DEQ (Drug Effects Scale) will not be taken into aspect in this thesis. BAL is the breath alcohol level and BP is the blood pressure.

Statistical methods

Data was collected on paper and manually transferred into Microsoft Excel where it was arranged and prepared before analysis. It was then transferred into GraphPad Prism 7 where graphs were created and into IBM SPSS v24.0 for statistical analysis. A 2-way ANOVA with the change-scores from BAES and POMS as dependent variables was used with ED and alcohol as fixed factors to investigate the effects of the drinks alone and in combination to reveal any possible interaction effects. When comparing effects between different treatments we adjusted the scores by subtracting the scores from the corresponding baselines. We used a probability value of 0.05 as cut-off for results to be significant for all analysis. To adjust for multiple comparisons, we used Bonferroni correction for confidence interval adjustment.

Results

Descriptive statistics with all mean scores for all subscales and for all time points can be found in Table 2 (see *Tables*). Two-way ANOVAs were performed on all measured subscales to look for differences in baseline scores. No significant differences could be found at baseline between the groups on any subscale. Analysis with two-way ANOVA of 'BAES Stimulation' at 20 minutes revealed a significantly higher score for alcohol when comparing the between-subjects effects [$F(1, 57) = 4.985$, $*p < .05$] (figure B in *Figures*).
Analysis with two-way ANOVA of 'BAES Stimulation' at 60 minutes showed no significant difference between any of the treatment groups (figure B in *Figures*). However, two-way ANOVA of 'BAES Sedation' at 20 minutes revealed a significantly higher score for alcohol [$F(1, 57) = 6.240$, $*p < .05$] (figure C in *Figures*) and a marginally significant interaction effect for alcohol and energy drink combined [$F(1, 57) = 3.981$, $p = .051$] (figure C in *Figures*). The two-way ANOVA of 'BAES Sedation' at 60 minutes revealed a significantly

higher score for alcohol [$F(1, 57) = 15.157$, ***$p < .001$] (figure C in *Figures*) and a significant interaction effect with increased score of alcohol and energy drink combined [$F(1, 57) = 4.246$, *$p < .05$] (figure C in *Figures*). When analyzing POMS data, two-way ANOVA of 'POMS Confusion' at 20 minutes revealed a marginally significant effect for alcohol [$F(1, 57) = 3.540$, $p = .065$] (figure D in *Figures*). The two-way ANOVA analysis of 'POMS Confusion' at 60 minutes revealed a significantly higher score for alcohol [$F(1, 57) = 7.760$, *$p < .01$] (figure D in *Figures*). However, analysis with two-way ANOVA of 'POMS Fatigue' (figure E in *Figures*), 'POMS Anger' (figure F in *Figures*), 'POMS Tension' (figure G in *Figures*), and 'POMS Depression' (figure H in *Figures*), 'POMS Vigour' (figure I in *Figures*), 'POMS Total Mood Disturbance' (figure J in *Figures*), revealed no significant effect on any of the time points between the different treatments.

Discussion and conclusions

The creators of BAES included two studies in their paper when assessing the validation of BAES for alcohol [75]. In the first study, prior to proceeding the experiment the writers first defined the AL. This was done by using BALs from subjects as a surrogate marker. The experimenters measured the subjects BAL 7 minutes after the consumption of the alcoholic beverages. Experiment leaders then measured the BAL again with 2 to 4-minute intervals until a rising level between 0.03% and 0.06% was achieved, which also defined the AL for that specific subject. The subject then completed BAES. BALs were measured in a repeated manner until the levels started to descend again. The DL was defined as the point where the level had dropped to the same as the level that defined the AL. This means that subjects performed BAES at an individually set time points depending on their BAL. Subjects had a mean ascending BAL of 0.052% and a mean descending BAL of 0.049% and the time ranged

from 71 to 149 minutes between the subjects AL and DL, supporting the fact of the individual differences in response to alcohol consumption. In our study we used a lower, weight adjusted dose of alcohol (0.4g/kg body weight) and fixed time intervals between measurements to investigate whether BAES was able to measure the biphasic effects of alcohol under these new conditions. Our results showed that BAES stimulation was significantly higher for alcohol during the AL but not during the DL even though we used a fixed time of 40 minutes between the AL and DL for all participants, supporting the hypothesis that BAES is usable in lower doses of alcohol. Also, the alcohol group reported higher scores on sedation during the DL with a strong statistical significance, further supporting the hypothesis. Sedation was also significantly higher for alcohol during AL but with a lower mean score than in the DL, just as in the BAES validation study. We therefore conclude that BAES is able to measure the stimulatory and sedative effects of alcohol in the AL and DL respectively, with fixed time intervals and at lower alcohol levels than those used in the validation study. The results of POMS revealed a significantly higher score in the alcohol group for confusion during the DL. Confusion is arguably the item of POMS that has the most similarities with the item sedation of BAES. This brings novel information that the original version of POMS is able to measure the effects of alcohol during the DL at low doses of alcohol with fixed time intervals. We conclude that POMS does not bring any additional information over BAES when measuring the acute effects of alcohol, ED or AmED, but that POMS is able to measure the acute effects of alcohol during the DL at low doses of alcohol with fixed time intervals. We found no measurable effects for ED alone with BAES or POMS. It is unclear whether ED alone causes any mood changes at all. If ED alone is able to alter mood, BAES and POMS are not the instruments of choice to measure these effects. However, a higher dose of ED could possibly had given different results.

Previous studies have shown inconclusive data regarding the subjective effects of mixing energy drinks with alcohol. For AmED, we found no enhancing effect of energy drink for alcohol on stimulation during the AL as in some previous studies [47, 48]. However, our results revealed a significant interaction effect between alcohol and energy drinks during the DL, with AmED drinkers reporting higher scores than alcohol drinkers on 'sedation'. The mechanisms behind this result we can only speculate on. The results from surveys report the opposite, that AmED increases the stimulative effects of alcohol and reduces its sedative effects [46, 78]. These effects have shown to be stronger with increasing doses of ED. Therefore, higher doses of ED in the present study could possibly have given a different result regarding the interaction [79]. However, clinical studies have to our knowledge never shown that AmED can reduce the sedative effects, i.e. how students use AmED to mask the sedative effects of alcohol when partying [12]. Also, it has been shown in clinical studies that caffeine alone can reduce the sedative effects of alcohol [80]. Some studies report no effects of AmED compared to alcohol alone on sedation, although these studies used a within-subjects statistical approach and a low ED dose (250 ml) which might have affected the results due to its dose dependet effect [47, 48, 51, 81]. Supporting our findings, one previous clinical study measured sedation-like effects and reported that AmED drinkers felt more 'drowsy', 'mentally slow' and 'clumsy' than alcohol drinkers [82]. The difference between results in surveys and clinical studies can possibly be explained by that AmED-drinkers don't report the same effects of AmED-intoxication when in a sober state, as when in an intoxicated state. Could it be that there is a discrepancy between how drinkers report their experience of the intoxication depending on when they report it? There is a risk of recall bias when subjects report the experienced effects of the mix a long time after consumption, as in the survey study [46]. This could explain the difference in how subjects report the effects of the mix, during consumption versus a long time (days or more) after consumption. Our results might bring

further understanding to why individuals that consume AmED are at increased risk of harm. If the AmED consumer anticipates becoming less sedated but instead becomes the opposite, the person might underestimate the level of intoxication, something that could lead to an increased intake of alcohol and in the end a high-risk behavior. However, the definite mechanism behind the discrepancy of how individuals report the mood-altering effects of AmED are not completely understood at the present time. With this knowledge, it is important for AmED users to be aware of the plausible risk of the combination and that the effects are not what the drinker often expects.

For a long time, it has been well known that individuals differ in how they respond to alcohol. There are multiple factors behind this phenomenon. Some factors have been explained such as the mood before drinking, time of last meal, time of day, sex, and other genetic factors that might affect both metabolism and response to alcohol intake [83-85]. There were no instructions to the participants regarding restrictions about the time of last meal prior to the experiment. Since the energy drink used in our study contained less carbohydrates than the ice tea used as placebo, the difference in carbohydrates could possibly have affected the ED and AmED-group in this manner. We here conclude that the interaction effect of AmED found on BAES sedation needs to be further studied, possibly even at higher doses of alcohol or energy drink. Also, subjects should be instructed about the time of last meal to reduce this possible confounder. Additionally, it would be optimal if all subjects received the same amounts of sugar. More studies are needed to further characterize the subjective effects of mixing alcohol and energy drink. It is essential to expand the knowledge of how these drinks affect the human brain to minimize the physical and psychiatric harm to young individuals all over the world.

Populärvetenskaplig sammanfattning (svenska)

De senaste decennierna har konsumtionen av energidryck ökat exponentiellt världen över och har idag kommit att utgöra en mångmiljardindustri med ungdomar som största målgrupp. Dryckernas innehåll av ämnen som exempelvis taurin och koffein har fått allt ifrån forskare till föräldrar och politiker att reagera eftersom fallrapporter och enkätstudier tyder på att individer som kombinerar alkohol och energidryck blir mer impulsiva, underskattar sin berusningsgrad, har en ökad risk för alkoholberoende, samt utsätter sig själva och andra för mer våld. Många säger sig dricka energidryck ihop med alkohol eftersom det kan minska alkoholens tröttande effekt. För att vidare kartlägga effekterna av kombinationen energidryck och alkohol valde vi att utforma en studie i en kontrollerad miljö. Vi ville undersöka ifall de två neuropsykiatriska frågeformulären ’Biphasic Alcohol Effects Scale’ (BAES) och ’Profile Of Mood States’ (POMS) kunde mäta skillnader i de upplevda effekterna av blandningen energidryck och alkohol, jämfört med alkohol ensamt. De båda formulären mäter olika känslor och tillstånd så som att känna sig stimulerad, trött och förvirrad. Vi rekryterade unga och friska personer, där den största andelen var studenter från Göteborgs Universitet. Samtliga kandidater genomgick en basal undersökning för att utesluta psykisk sjukdom och allvarligare fysisk sjukdom. Efter exklusion kvarstod totalt 61 försökspersoner som efter en randomiseringsprocess tilldelades en av fyra följande drycker eller dryckeskombinationer; 1. Placebo (Lipton® Iced Tea), 2. Energidryck (Monster Energy Rehab®), 3. Kombinationen placebo och alkohol (0,4g alkohol per kg kroppsvikt i form av Absolut Vodka®), 4. Kombinationen energidryck och alkohol. Genom självskattning fick försökspersonerna fylla i de båda formulären, vilket genomfördes av samtliga deltagare vid tre olika tidpunkter; innan dryck, 20 minuter efter intag, samt 60 minuter efter intag. Resultaten visade att BAES kunde mäta alkoholens effekter precis som förväntat. POMS kunde inte tillföra någon ytterligare

information utöver BAES. Vi kunde inte påvisa några mätbara effekter av energidryck ensamt. Det är oklart om energidryck har några effekter över huvud taget. Kombinationen av alkohol och energidryck visade däremot på en interaktionseffekt där de som drack kombinationen upplevde sig mer trötta än de som bara drack alkohol, trots att enkätstudier tyder på det motsatta. Vi hypotiserar att det finns en skillnad i hur personer rapporterar effekterna beroende på när de tillfrågas. Det verkar som att kombinationen alkohol och energidryck under tiden för konsumtion gör personen mer trött, men att personen i ett senare skede (dagar eller mer) beskriver det motsatta. Resultatet skulle kunna förklara hur kombinationen alkohol och energidryck ökar risken för både fysisk och psykisk skada genom att det finns en förväntanseffekt hos den som dricker. Om individen förväntar sig att bli mindre trött av alkohol men tvärtom blir mer trött, skulle det kunna leda till att individen dricker mer alkohol och därmed har en ökad risk för ohälsa. Mekanismen bakom resultatet är i nuläget oklart och det krävs fortsatta studier, förslagsvis med högre koncentration alkohol och energidryck för att bättre förstå hur blandningen av dessa drycker påverkar den mänskliga hjärnan.

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Tables

Table 1. Demographic characteristics for the included subjects. After randomization subjects were placed in one of the following treatment groups: 1. Placebo (Lipton® Ice Tea Lemon 7.14 ml/kg body weight), 2. Energy drink (Monster® Rehab Lemonade 7.14 ml/kg body weight), 3. Placebo + alcohol (Absolut Vodka® (40%) 0.4 g alcohol/kg body weight), 4. Energy drink + alcohol. The table displays occupation, earlier drug use, current use of alcohol, energy drink, nicotine and coffee. Family history of alcoholism (extending 1 or 2 generations) is also displayed. Before enrollment all subjects performed AUDIT, scores of which are also presented in this table.

TOTAL	placebo	ENERGY DRINK	ALCOHOL	ALCOHOL + ENERGY DRINK
(*N* = 61)	(*n* = 14)	(*n* = 15)	(*n* = 16)	(*n* = 16)
Age, *years, range*	21-28	19-34	20-30	18-34
(mean ± SEM)	24.4 ± 0.5	25.5 ± 1.1	24.2 ± 0.7	25.6 ± 1.0
Height, *cm* (mean ± SEM)	170.9 ± 2.3	172.7 ± 2.7	175.2 ± 2.1	174.6 ± 2.9
Weight, *kg* (mean ± SEM)	66.2 ± 2.3	66.7 ± 3.2	72.7 ± 2.7	67.4 ± 3.2
BMI (mean ± SEM)	22.6 ± 0.6	22.2 ± 0.7	23.6 ± 0.6	21.9 ± 0.6
Gender, *n*				
Male	5	7	10	9
Female	9	8	6	7
Occupation, *n*				
Full time student	13	12	14	13
Full time employment	1	2	2	3
Unemployed	0	1	0	0
Current use, *n* (weekly)				
Alcohol	14	15	16	16
Energy drink	2	0	3	3
Nicotine	3	4	2	2
Coffee	9	13	15	13
Lifetime drug use, *n*				
Stimulants	0	1	1	2
Tranquilizers	2	1	2	2
Hallucinogenes	0	0	0	0
Opiates	0	0	0	0
Marijuana	6	7	8	6
Family history of alcoholism, *n*	1	5	2	2
AUDIT, *points* (mean ± SEM)	5.3 ± 0.6	5.4 ± 0.5	5.4 ± 0.7	5.6 ± 0.7

AUDIT = Alcohol Use Disorders Identification Test

Table 2. Descriptive statistics of the results from the two neuropsychological questionnaires BAES and POMS for all groups, subscales and measured time points; baseline, 20 minutes' post drink administration, and 60 minutes' post drink administration. The table shows mean scores and standard error of the mean (SEM).

	placebo			ENERGY DRINK			ALCOHOL			ALCOHOL + ENERGY DRINK		
Subscale	baseline	20 min	60 min	baseline	20 min	60 min	baseline	20 min	60 min	baseline	20 min	60 min
BAES Stimulation												
Mean	20,8	20,8	17,5	26,0	26,4	24,5	25,8	31,1	24,5	26,4	32,8	29,3
SEM	2,9	3,5	3,0	3,0	3,4	2,8	4,0	3,3	3,1	2,3	1,5	1,7
BAES Sedation												
Mean	7,8	8,6	7,1	15,1	10,6	8,7	9,8	11,8	13,1	8,7	13,9	15,4
SEM	1,7	1,6	1,5	3,0	2,1	2,1	2,5	2,6	2,5	2,0	2,6	3,0
POMS Confusion												
Mean	6,1	6,1	5,7	5,3	5,5	4,9	5,1	6,3	5,9	6,1	8,3	8,4
SEM	1,2	1,4	1,4	0,9	0,9	0,8	0,7	1,0	0,6	0,7	1,1	1,2
POMS Fatigue												
Mean	7,4	5,5	5,4	6,2	4,9	4,2	6,1	5,8	5,4	6,2	5,1	6,5
SEM	1,4	1,5	1,6	1,1	1,1	1,0	1,1	1,8	1,1	1,2	1,1	1,4
POMS Anger												
Mean	4,1	2,2	1,9	3,1	2,9	2,4	3,1	3,1	1,5	3,2	1,4	1,8
SEM	1,6	1,2	1,1	0,9	1,0	1,4	1,0	1,5	0,6	1,0	0,6	0,6
POMS Tension												
Mean	7,9	6,5	5,9	6,0	6,1	5,7	6,6	5,9	4,6	7,1	4,7	5,0
SEM	2,1	1,5	1,9	0,7	1,3	0,7	1,1	1,5	0,9	0,9	0,7	1,0
POMS Depression												
Mean	7,1	5,5	5,6	5,6	3,9	4,1	2,4	3,9	1,8	2,4	0,9	2,4
SEM	3,6	3,3	3,5	2,4	2,1	2,0	0,9	2,7	1,0	0,8	0,4	0,9
POMS Vigour												
Mean	14,1	13,7	12,6	14,3	15,4	14,9	16,0	16,1	14,6	15,6	14,3	14,6
SEM	1,6	1,8	1,6	1,2	1,5	1,3	1,3	1,5	1,2	1,4	1,5	1,4
POMS TMD												
Mean	18,4	12,1	11,9	11,8	7,8	6,3	7,3	8,8	4,6	9,4	6,1	9,5
SEM	10,2	8,3	9,4	6,2	6,0	5,5	3,7	8,1	3,6	4,0	3,7	5,2

BAES = Biphasic Alcohol Effects Scale
POMS = Profile Of Mood States

Figures

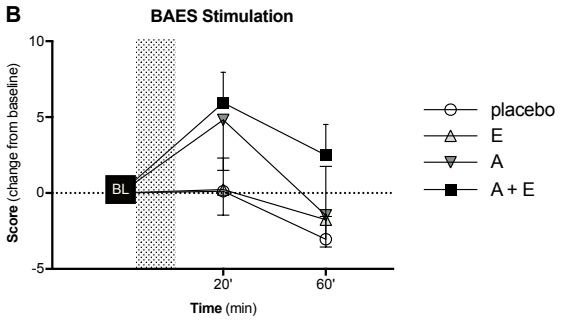

Figure B. Displaying the score in change from baseline (BL) for BAES Stimulation. The shadowed area represents the time of drink consumption. Placebo is the group treated with ice tea. E is the group treated with energy drink. A is the group treated with alcohol and ice tea. A + E is the group treated with alcohol and energy drink. Analysis with two-way at 20 minutes (change from baseline) revealed a significantly higher score for alcohol when comparing the between-subjects effects [$F(1, 57) = 4.985$, $*p < .05$]. No significant effects could be found at 60 minutes.

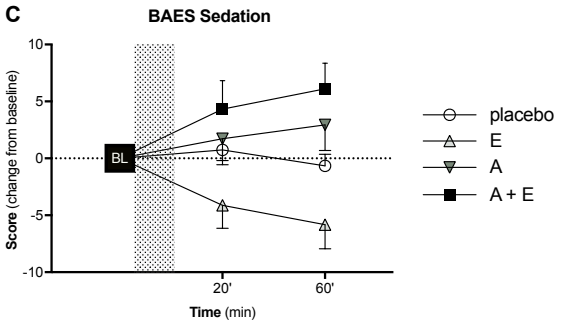

Figure C. Displaying the score in change from baseline (BL) for BAES Sedation. The shadowed area represents the time of drink consumption. Placebo is the group treated with ice tea. E is the group treated with energy drink. A is the group treated with alcohol and ice tea. A + E is the group treated with alcohol and energy drink. Analysis with two-way ANOVA at 20 minutes revealed a significantly higher score for alcohol [$F(1, 57) = 6.240$, $*p < .05$] and a marginally significant interaction effect for alcohol and energy drink combined [$F(1, 57) = 3.981$, $p = .051$]. Analysis with two-way ANOVA at 60 minutes revealed a significantly higher score for alcohol [$F(1, 57) = 15.157$, $***p < .001$] and a significant interaction effect with increased score of alcohol and energy drink combined [$F(1, 57) = 4.246$, $*p < .05$].

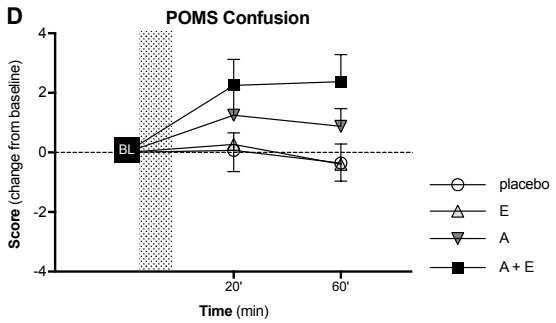

Figure D. Displaying the score in change from baseline (BL) for POMS Confusion. The shadowed area represents the time of drink consumption. Placebo is the group treated with ice tea. E is the group treated with energy drink. A is the group treated with alcohol and ice tea. A + E is the group treated with alcohol and energy drink. Analysis with two-way ANOVA at 20 minutes revealed a marginally significant effect for alcohol [$F(1, 57) = 3.540$, $p = .065$]. Analysis with two-way ANOVA at 60 minutes revealed a significantly higher score for alcohol [$F(1, 57) = 7.760$, $**p < .01$].

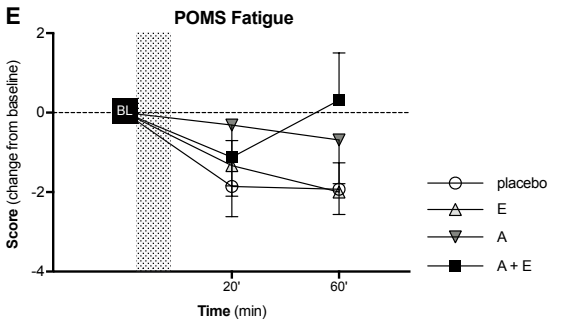

Figure E. Displaying the score in change from baseline (BL) for POMS Fatigue. The shadowed area represents the time of drink consumption. Placebo is the group treated with ice tea. E is the group treated with energy drink. A is the group treated with alcohol and ice tea. A + E is the group treated with alcohol and energy drink. Analysis with two-way ANOVA revealed no significant effect on any of the time points between the different treatments.

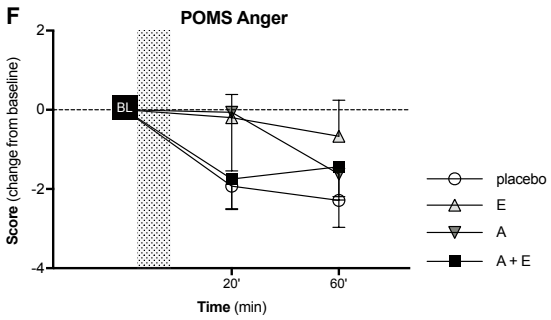

Figure F. Displaying the score in change from baseline (BL) for POMS Anger. The shadowed area represents the time of drink consumption. Placebo is the group treated with ice tea. E is the group treated with energy drink. A is the group treated with alcohol and ice tea. A + E is the group treated with alcohol and energy drink. Analysis with two-way ANOVA revealed no significant effect on any of the time points between the different treatments.

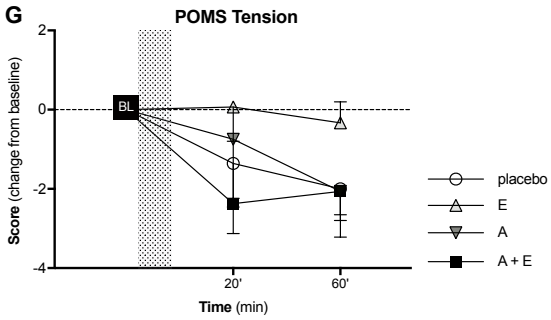

Figure G. Displaying the score in change from baseline (BL) for POMS Tension. The shadowed area represents the time of drink consumption. Placebo is the group treated with ice tea. E is the group treated with energy drink. A is the group treated with alcohol and ice tea. A + E is the group treated with alcohol and energy drink. Analysis with two-way ANOVA revealed no significant effect on any of the time points between the different treatments.

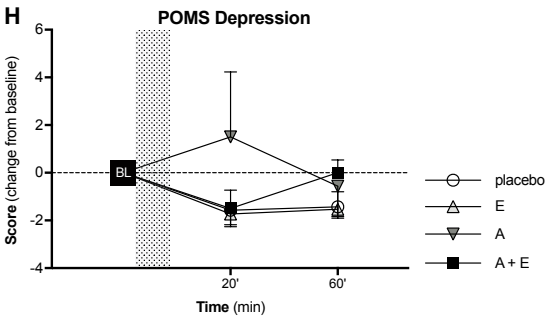

Figure H. Displaying the score in change from baseline (BL) for POMS Depression. The shadowed area represents the time of drink consumption. Placebo is the group treated with ice tea. E is the group treated with energy drink. A is the group treated with alcohol and ice tea. A + E is the group treated with alcohol and energy drink. Analysis with two-way ANOVA revealed no significant effect on any of the time points between the different treatments.

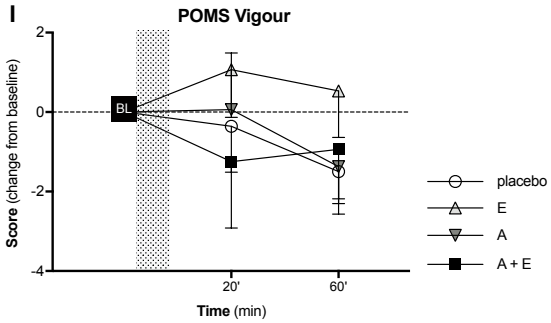

Figure I. Displaying the score in change from baseline (BL) for POMS Vigour. The shadowed area represents the time of drink consumption. Placebo is the group treated with ice tea. E is the group treated with energy drink. A is the group treated with alcohol and ice tea. A + E is the group treated with alcohol and energy drink. Analysis with two-way ANOVA revealed no significant effect on any of the time points between the different treatments.

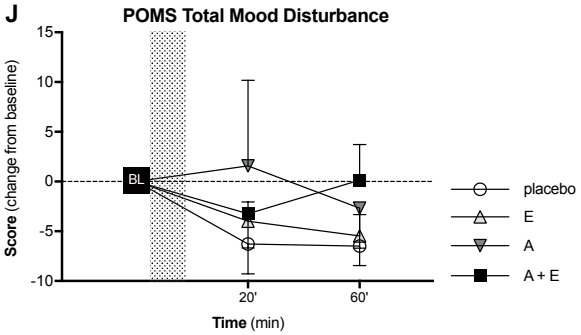

Figure J. Displaying the score in change from baseline (BL) for POMS Total Mood Disturbance. The shadowed area represents the time of drink consumption. Placebo is the group treated with ice tea. E is the group treated with energy drink. A is the group treated with alcohol and ice tea. A + E is the group treated with alcohol and energy drink. Analysis with two-way ANOVA revealed no significant effect on any of the time points between the different treatments.

APPENDIX A – Symptom Checklist 90

SCL 90

Namn_____ _____ Nummer_____

Datum_____ Ålder/födelsedatum_____

INSTRUKTION

Nedan följer en lista över problem och besvär som man ibland har. Listan består av 90 olika påståenden. Läs noggrant igenom ett i taget och ringa därefter in siffran till höger som visar hur mycket problemet ifråga har besvärat Dig **den senaste veckan.**

Markera alltså med en ring det alternativ (0-4), som Du tycker bäst beskriver hur Du känt det under det senaste 7 dagarna. Markera bara **ett** alternativ för varje påstående och försäkra Dig om att Du inte hoppar över något.

Studera exemplet nedan innan Du börjar.

EXEMPEL:
Hur mycket har Du besvärats av:

	Inte alls	Lite grand	Måttligt	Ganska mycket	Väldigt mycket
1. Ont i ryggen	0	1	2	3	4

Hur mycket har Du besvärats av:	Inte alls	Lite grand	Måttligt	Ganska mycket	Väldigt mycket
1. Huvudvärk	0	1	2	3	4
2. Nervositet eller inre oro	0	1	2	3	4
3. Återkommande tankar, ord eller idéer, som Du inte kan göra Dig fri från	0	1	2	3	4
4. Svimningskänsla eller yrsel	0	1	2	3	4
5. Förlust av sexuellt intresse eller njutning	0	1	2	3	4
6. Att känna Dig kritisk mot andra	0	1	2	3	4
7. Känsla av att någon annan kan kontrollera Dina tankar	0	1	2	3	4
8. Känsla av att andra är skuld till de flesta av Dina problem	0	1	2	3	4
9. Svårigheter att komma ihåg saker och ting	0	1	2	3	4
10. Oro över slarv eller vårdslöhet	0	1	2	3	4
11. Att Du lätt blir förargad eller irriterad	0	1	2	3	4

Hur mycket har Du besvärats av:	Inte alls	Lite grand	Måttligt	Ganska mycket	Väldigt mycket
12. Smärtor i hjärttrakten eller i bröstet	0	1	2	3	4
13. Att känna Dig rädd när Du vistas på öppna platser eller på gator	0	1	2	3	4
14. Tröghet eller brist på energi	0	1	2	3	4
15. Tankar på att ta Ditt liv	0	1	2	3	4
16. Att höra röster som andra människor inte hör	0	1	2	3	4
17. Att känna Dig darrig	0	1	2	3	4
18. En känsla av att de flesta människor inte går att lita på	0	1	2	3	4
19. Dålig aprit	0	1	2	3	4
20. Att ha lätt för att brista i gråt0	1	2	3	4	
21. Att Du känner Dig blyg eller besvärad inför det motsatta könet	0	1	2	3	4
22. Känslan av att vara snärjd eller fångad	0	1	2	3	4
23. Att plötsligt känna Dig rädd utan anledning	0	1	2	3	4
24. Okontrollerbara utbrott av ilska	0	1	2	3	4
25. Rädsla för att gå hemifrån ensam	0	1	2	3	4
26. Att klandra Dig själv för saker och ting	0	1	2	3	4
27. Smärtor i nedre delen av ryggen	0	1	2	3	4
28. Att har svårt att få saker och ting gjorda	0	1	2	3	4
29. Ensamhetskänslor	0	1	2	3	4
30. Nedstämdhet	0	1	2	3	4
31. Alltför mycket oro för saker och ting	0	1	2	3	4
32. Brist på intresse för saker och ting	0	1	2	3	4
33. Rädsla och ängslighet	0	1	2	3	4
34. Att bli lätt sårad	0	1	2	3	4
35. Känslan av att andra vet vad Du tänker	0	1	2	3	4
36. En känsla av att andra inte förstår Dig eller inte bryr sig om Dig	0	1	2	3	4

Hur mycket besväras du av:	Inte Alls	Lite grand	Måttligt	Ganska mycket	Väldigt mycket
37. Att känna att andra är ovänliga eller tycker illa om Dig	0	1	2	3	4
38. Att behöva göra saker och ting mycket långsamt för att vara säker på att det blir rätt	0	1	2	3	4
39. Hjärtklappning eller andra obehags-känslor från hjärtat	0	1	2	3	4
40. Illamående eller orolig mage0	1	2	3	4	
41. Att du känner Dig underlägsen andra	0	1	2	3	4
42. Värk eller ömhet i musklerna	0	1	2	3	4
43. Känslan av att andra iakttar Dig eller pratar om Dig	0	1	2	3	4
44. Svårigheter att somna	0	1	2	3	4
45. Att Du måste kontroller vad Du gör gång på gång	0	1	2	3	4
46. Att har svårt för att bestämma Dig	0	1	2	3	4
47. Rädsla på att åka med tåg, buss, spår-vagn eller tunnelbana	0	1	2	3	4
48. Att ha svårt att andas	0	1	2	3	4
49. Vågor av kyla eller värme genom kroppen	0	1	2	3	4
50. Att Du måste undvika vissa saker, platser eller aktiviteter, därför att de skrämmer dig	0	1	2	3	4
51. En känsla av tomhet i huvudet	0	1	2	3	4
52. Att det domnar eller sticker i olika delar av kroppen	0	1	2	3	4
53. En känsla av en klump i halsen	0	1	2	3	4
54. Känslor av hopplöshet inför framtiden	0	1	2	3	4
55. Koncentrationssvårigheter	0	1	2	3	4
56. Svaghet i delar av kroppen	0	1	2	3	4
57. Att Du känner Dig spänd eller uppjagad	0	1	2	3	4
58. Att du känner Dig tung i armar eller ben	0	1	2	3	4
59. Tankar på döden och hur det är att dö	0	1	2	3	4

Hur mycket besväras du av:	Inte Alls	Lite grand	Måttlig	Ganska mycket	Väldigt mycket
60. Att Du äter för mycket	0	1	2	3	4
61. Obehag, när andra iakttar Dig eller pratar om Dig	0	1	2	3	4
62. Tankar, som inte är Dina egna	0	1	2	3	4
63. Impulser att slå, skada eller göra någon illa	0	1	2	3	4
64. Att vakna tidigt på morgonen	0	1	2	3	4
65. Handlingar som Du måste upprepa flera gånger eller utföra efter ett bestämt mönster (t.ex. röra vid vissa saker, tvätta Dig eller räkna)	0	1	2	3	4
66.Orolig eller störd sömn	0	1	2	3	4
67. Impulser att slå sönder eller krossa saker	0	1	2	3	4
68. Idéer eller övertygelser, som andra inte delar	0	1	2	3	4
69. Att känna Dig mycket osäker och generad tillsammans med andra människor	0	1	2	3	4
70. Obehag när Du vistas bland mycket folk (t.ex. i affärer eller på biografer)	0	1	2	3	4
71. Att allt känns ansträngande	0	1	2	3	4
72. Ångest- eller panikattacker	0	1	2	3	4
73. Obehag att dricka eller äta ute (t.ex. på barer eller restauranger)	0	1	2	3	4
74. Att ofta hamna i häftiga ordväxlingar	0	1	2	3	4
75. Att känna Dig nervös, när Du är ensam	0	1	2	3	4
76. Att andra inte tillräckligt uppskattar det Du gör	0	1	2	3	4
7.7 Att Du känner Dig ensam även när Du är tillsammans med andra	0	1	2	3	4
78. Oro och rastlöshet så att Du inte kan sitta still	0	1	2	3	4
79. Känslor av att vara värdelös	0	1	2	3	4
80. Känslan att välbekanta saker är underliga eller overkliga	0	1	2	3	4

Hur mycket besväras du av:	Inte Alls	Lite grand	Måttligt	Ganska mycket	Väldigt mycket
81. Att du skriker eller kastar saker	0	1	2	3	4
82. Rädsla för att svimma när Du vistas ute bland folk	0	1	2	3	4
83. Känslan att folk skulle utnyttja Dig om de kunde	0	1	2	3	4
84. Sexuella tankar oroar Dig mycket	0	1	2	3	4
85. Tankar att Du borde bli straffad för dina synder	0	1	2	3	4
86. Att känna Dig pressad att få saker gjorda	0	1	2	3	4
87. Känslan att Du har något allvarligt kroppslig fel	0	1	2	3	4
88. Att aldrig känna Dig nära någon annan människa	0	1	2	3	4
89. Skuldkänslor	0	1	2	3	4
90. Föreställningen att det är något fel på Ditt förstånd	0	1	2	3	4

Tack för hjälpen.

APPENDIX B – Alcohol use disorders identification test

AUDIT

Här är ett antal frågor om Dina alkoholvanor

Vi är tacksamma om Du besvarar dem så noggrant och ärligt som möjligt genom att markera det alternativ som gäller för Dig.

Med ett ”glas” menas:


50 cl folköl


33 cl starköl


1 glas rött el vitt vin


1 litet glas starkvin


4 cl sprit, t. ex. whisky

Hur gammal är du? ☐☐ **år** **Man** ☐ **Kvinna** ☐

1.	Hur ofta dricker Du alkohol?	Aldrig ☐	1 gång i månaden eller mer sällan ☐	2-4 gånger i månaden ☐	2-3 gånger i veckan ☐	4 gånger/vecka eller mer ☐
2.	Hur många ”glas” (se exempel) Dricker Du en typisk dag då Du dricker alkohol?	1 - 2 ☐	3 - 4 ☐	5 – 6 ☐	7 – 9 ☐	10 eller fler ☐
3.	Hur ofta dricker Du *sex* sådana ”glas” eller *mer* vid samma tillfälle?	Aldrig ☐	Mer sällan än en gång i månaden ☐	Varje månad ☐	Varje vecka ☐	Dagligen eller nästan varje dag ☐
4.	Hur ofta under det senaste året har Du inte kunnat sluta dricka sedan Du börjat?	Aldrig ☐	Mer sällan än en gång i månaden ☐	Varje månad ☐	Varje vecka ☐	Dagligen eller nästan varje dag ☐
5.	Hur ofta under det senaste året har Du låtit bli att göra något som Du borde för att Du drack?	Aldrig ☐	Mer sällan än en gång i månaden ☐	Varje månad ☐	Varje vecka ☐	Dagligen eller nästan varje dag ☐
6.	Hur ofta under senaste året har Du behövt en ”drink” på morgonen efter mycket drickande dagen innan?	Aldrig ☐	Mer sällan än en gång i månaden ☐	Varje månad ☐	Varje vecka ☐	Dagligen eller nästan varje dag ☐
7.	Hur ofta under det senaste året har Du haft skuldkänslor eller samvets-förebråelser på grund av Ditt drickande?	Aldrig ☐	Mer sällan än en gång i månaden ☐	Varje månad ☐	Varje vecka ☐	Dagligen eller nästan varje dag ☐
8.	Hur ofta under det senaste året har Du druckit så att Du dagen efter inte kommit ihåg vad Du sagt eller gjort?	Aldrig ☐	Mer sällan än en gång i månaden ☐	Varje månad ☐	Varje vecka ☐	Dagligen eller nästan varje dag ☐
9.	Har Du eller någon annan blivit skadad på grund av Ditt drickande?	Nej ☐	Ja, men inte under det senaste året ☐			Ja, under det senaste året ☐
10.	Har en släkting eller vän, en läkare (eller någon annan inom sjukvården) oroat sig över Ditt drickande eller antytt att Du borde minska på det?	Nej ☐	Ja, men inte under det senaste året ☐			Ja, under det senaste året ☐

Översatt och bearbetat av prof. Hans Bergman, Karolinska Institutet, Stockholm

Har Du besvarat alla frågor? - Tack för Din medverkan!

APPENDIX C – Biphasic alcohol effects scale

The following adjectives describe feelings that some people have after drinking alcohol. Please rate the extent to which drinking alcohol has produced these feelings in you at the present time.

1) Difficulty Concentrating

0 1 2 3 4 5 6 7 8 9 10

(not at all) (extremely)

2) Down

0 1 2 3 4 5 6 7 8 9 10

(not at all) (extremely)

3) Elated

0 1 2 3 4 5 6 7 8 9 10

(not at all) (extremely)

4) Energized

0 1 2 3 4 5 6 7 8 9 10

(not at all) (extremely)

5) Excited

0 1 2 3 4 5 6 7 8 9 10

(not at all) (extremely)

6) Heavy head

0 1 2 3 4 5 6 7 8 9 10

(not at all) (extremely)

7) Inactive

0 1 2 3 4 5 6 7 8 9 10

(not at all) (extremely)

8) Sedated

0 1 2 3 4 5 6 7 8 9 10

(not at all) (extremely)

9) Slow thoughts

0 1 2 3 4 5 6 7 8 9 10

(not at all) (extremely)

10) Sluggish

0 1 2 3 4 5 6 7 8 9 10

(not at all) (extremely)

11) Stimulated

0 1 2 3 4 5 6 7 8 9 10

(not at all) (extremely)

12) Talkative

0 1 2 3 4 5 6 7 8 9 10

(not at all) (extremely)

13) Up

0 1 2 3 4 5 6 7 8 9 10

(not at all) (extremely)

14) Vigorous

0 1 2 3 4 5 6 7 8 9 10

(not at all) (extremely)

APPENDIX D – Profile of mood states

Profile of Mood States

Subject's Initials

Birth date

Date

Subject Code No.

Directions: Describe HOW YOU FEEL RIGHT NOW
by circling the most appropriate number after each of the words listed below:

FEELING	Not at all	A little	Moderate	Quite a bit	Extremely
1. Friendly	1	2	3	4	5
2. Tense	1	2	3	4	5
3. Angry	1	2	3	4	5
4. Worn Out	1	2	3	4	5
5. Unhappy	1	2	3	4	5
6. Clear-headed	1	2	3	4	5
7. Lively	1	2	3	4	5
8. Confused	1	2	3	4	5
9. Sorry for things done	1	2	3	4	5
10. Shaky	1	2	3	4	5
11. Listless	1	2	3	4	5
12. Peeved	1	2	3	4	5
13. Considerate	1	2	3	4	5
14. Sad	1	2	3	4	5
15. Active	1	2	3	4	5
16. On edge	1	2	3	4	5
17. Grouchy	1	2	3	4	5
18. Blue	1	2	3	4	5
19. Energetic	1	2	3	4	5
20. Panicky	1	2	3	4	5
21. Hopeless	1	2	3	4	5
22. Relaxed	1	2	3	4	5
23. Unworthy	1	2	3	4	5
24. Spiteful	1	2	3	4	5
25. Sympathetic	1	2	3	4	5
26. Uneasy	1	2	3	4	5
27. Restless	1	2	3	4	5
28. Unable to	1	2	3	4	5
29. Fatigued	1	2	3	4	5

30. Helpful	1	2	3	4	5
31. Annoyed	1	2	3	4	5
32. Discouraged	1	2	3	4	5
33. Resentful	1	2	3	4	5
34. Nervous	1	2	3	4	5
35. Lonely	1	2	3	4	5
36. Miserable	1	2	3	4	5
37. Muddled	1	2	3	4	5
38. Cheerful	1	2	3	4	5
39. Bitter	1	2	3	4	5
40. Exhausted	1	2	3	4	5
41. Anxious	1	2	3	4	5
42. Ready to fight	1	2	3	4	5
43. Good-natured	1	2	3	4	5
44. Gloomy	1	2	3	4	5
45. Desperate	1	2	3	4	5
46. Sluggish	1	2	3	4	5
47. Rebellious	1	2	3	4	5
48. Helpless	1	2	3	4	5
49. Weary	1	2	3	4	5
50. Bewildered	1	2	3	4	5
51. Alert	1	2	3	4	5
52. Deceived	1	2	3	4	5
53. Furious	1	2	3	4	5
54. Effacious	1	2	3	4	5
55. Trusting	1	2	3	4	5
56. Full of pep	1	2	3	4	5
57. Bad-tempered	1	2	3	4	5
58. Worthless	1	2	3	4	5
59. Forgetful	1	2	3	4	5
60. Carefree	1	2	3	4	5
61. Terrified	1	2	3	4	5
62. Guilty	1	2	3	4	5
63. Vigorous	1	2	3	4	5
64. Uncertain about things	1	2	3	4	5
65. Bushed	1	2	3	4	5