Energy drinks

Getting energy of the unknown

Masteressay

In collaboration with:
Faculty of mathematics & Natural sciences

Chris Vinke (1648454)

Supervised by:
Eddy van der Zee

22th of April 2014, Groningen

Abstract

In this demanding world, beverages enhancing cognition and decreasing sleepiness are gaining more and more popularity. Those energy drinks (EDs) contain caffeine, taurine, glucose, vitamins and herbal supplements. Although manufactures claim that EDs have a boosting effect, it is unclear whether those effects are caused by the supplements of EDs only or solely by the effect of caffeine. ED cans of 330 mL contain around 40 – 150 mg of caffeine, which is the same amount of caffeine present in coffee. These doses of caffeine can have a boosting effect on cognition. There is not much evidence about taurine, vitamins and the herbs having a positive or negative effect on the consumers' body. Mechanisms of those supplements are poorly understood, this essay was established to unravel the effects of EDs and to find the possible mechanisms of the ingredients incorporated in the EDs. The following questions were postulated to give answer about the effect of EDs on brain and heart function, *"Could energy drinks have an effect on ageing of the consumers?"* and *"What is the impact of the contents of energy drinks on the stress response of consumers?".* To answer those questions, a literature search was done by using PubMed, Web of Science and Google Scholar. Caffeine seems to have positive effects on brain function; nevertheless at high doses this effect could be reversed. The effect of taurine in EDs has not been studied appropriate but knowing that the blood brain barrier will not let taurine pass it suggests there is no effect on brain function. Glucose on its own could have an effect on the cells of humans but in EDs it has not been reported yet. Well structured studies revealing the mechanisms of all of the ED supplements have to be tested on their own as well as interaction studies between the supplements have to be done. Not only claims could be supported or rejected but also long term effects of EDs on the consumers can be established.

Table of contents

1 Introduction

1.1 Background

Humans need to drink enough fluids to maintain their internal water balance. Men have to drink at least 3 liters of beverages and women need to drink 2.2 liters of beverages a day, stated by the Institute of Medicine from the United States. The popularity of one of these beverages has risen since the 1960s, namely the category of sugary drinks containing caffeine, taurine, glucose and herbs called energy drinks (ED's). The interactions of all those substances are not tested yet.

Manufacturers of the ED's claim that the drinks improve mental condition, reaction speed and metabolism after consumption (Grasser *et al*., 2013) mostly because of the alkaloid caffeine, which can stimulate cognition but could lead to an increase in blood pressure (BP) and heart rate (Ishak *et al.,* 2012*)*. The combination of caffeine and the high amounts of glucose in ED's could further improve the cognitive performance and individual sleepiness throughout long periods of cognitive demand.

In this research field, there is scientific evidence in favor of the manufacturer's claims and against the health claims. Several studies do not show direct effects of ED's on the cardiovascular system. For examples, 45 minutes after consuming a capsule containing the same amounts of caffeine and taurine in ED's of 250 mL, no difference in heart rate or blood pressure was reported (Bichler *et al.*, 2006). On the other hand studies found an increase in BP without a change in heart rate at one hour post-drink of ED (250 mL) compared to a water control (250 mL) (Worthley *et al*., 2010). Another research team found with consumption of 500 mL of ED, resulted in an increase in heart rate as well as in the blood pressure at 2 hours and 4 hours after drinking (Steinke *et al*., 2009).

1.2 Project motive

After recent incidents occurring around the globe caused by drinking multiple ED's in a short amount of time, more people are wondering about the short and long term effects of the ED's. Because of the high popularity of ED's, potential health consequences should be tested and made public in an appropriate overview of the effects of ED's to fully understand the risks of those beverages (Reissig *et al.,* 2009). However, the number of publications of potential risks related to ED's is small. Here, I link most related articles and review the current knowledge regarding ED's. In addition, I connect research of the ageing cerebral and cardiovascular cells with the use of ED's. To define the word ageing in the context of the report, the decrease of brain function over time.

1.3 Research questions

To present the latest knowledge of ED's and address the main question in this field, "*What is the effect of the ingredients in energy drinks on the cerebral and heart function?",* literature searches were conducted using PubMed, Google Scholar and Web of Science including the keywords energy drink in combination with caffeine, taurine, glucose and ageing but the keyword searches were also performed separately. Glucose pathways and stress responses are well documented and can be connected to ageing research. To connect this research to ageing field the following questions are formulated:
Could energy drinks have an effect on ageing of the consumers?
What is the impact of the contents of energy drinks on the stress response of consumers?

2 Ingredients of energy drinks

Caffeine is suggested to be the active component of ED, and could be responsible for mental and behavioral effects. Also caffeine is the best documented ingredient of ED's; it can act as a thermogenic, ergogenic and as the 'energy boost'. But ED's do not only contain caffeine, table 1 illustrates the most important ingredients of different ED brands. Information about the ingredients is needed to get a better insight about the claims and the resistance against energy drinks. Not all experiments have been done with the same amounts of ingredients.

Table 1: Ingredients of ED's and their quantaties (Adapted from Ishak *et al., 2012).*

Contents per serving	Red Bull	Monster	Rockstar	Full Throttle	Sobe no fear
Caffeine	80mg	80mg	80mg	141mg	32mg
Taurine	ND	1000mg	1000mg	ND	ND
Sugar	27g	27g	31g	57g	27g
Guarana	ND	ND	25mg	ND	ND
Sodium	200mg	180mg	40mg	160mg	15mg
Vitamin B6	5mg	2mg	2mg	4mg	ND

ND=not disclosed

2.1 Caffeine

When people drink a beverage containing caffeine (1, 3, 7-trimethylxanthine), it will be absorbed from the gastrointestinal tract into the bloodstream and will become metabolized in the liver (Nawrot *et al*., 2003). Three major metabolites are formed during this process, paraxanthine (1,7-dimethylxanthine / 84%), theobromine (3,7-dimethylxanthine / 12%), and theophylline (1,3-dimethylxanthine / 4%), which have a similar chemical structure compared to caffeine (Safranow *et al.,* 2005).

After drinking a coffee or soft drink containing caffeine, caffeine will work as an adenosine receptor antagonist in the brain (Dunwiddie *et al.,* 2001). Adenosine and caffeine have a similar molecular structure, but caffeine can occupy the adenosine receptor (Fisone *et al.,* 2004). This means that by the blockage of adenosine interacting with the receptor, sleep promoting effects of adenosine cease to exist, which leads to being wakeful (Ferre, 2008).

When taking in a dose of 70 to 100 mg of caffeine the clearance of caffeine in the liver will be linear, but when obtained in a higher dose of 250 – 500 mg the clearance is affected extending the elimination of caffeine (Kaplan *et al.,* 1997). Studies verify the ability of caffeine to improve mood and alertness (Lorist *et al.,* 2003), exercise performance (Doherty *et al.,* 2004), information processing, alertness and reaction time (Cysneiros *et al.* 2007). Other research confirms the health benefits of caffeine in coffee and their relation to one another.

Negative effects of caffeine are disturbed sleeping patterns of children, which have swallowed caffeine, and could impair the development of the child. Studies with children or adolescents taking too much caffeine, at least 1.5 L of cola drinks per day (192.88 mg of caffeine daily), and an average of 11 L (range 10.5 to 21 L) of cola drinks a week, which average 1414.5 mg of caffeine may suffer from caffeine-induced daily headaches. Gradual withdrawal was achieved leading to complete cessation of all headaches (Hering-Hanit *et al.,* 2003). Other components than caffeine present in ED's should not be ignored.

2.2 Taurine

The second ingredient described is taurine (2-aminoethane- sulfonic acid), is a non-essential amino acid found in high concentrations in the brain, heart, and skeletal muscle (Huxtable *et al*., 1992). Taurine has multiple functions in the body, namely cell volume regulation, osmoregulation, anti-inflammatory activity, and it modulates the concentration of free intracellular calcium (Ripps *et al., 2012)*. Modulation of free calcium by taurine happens by protecting the body cells from glutamate toxicity through inhibiting glutamate overload. Taurine can also act as a neuromodulator; it functions as an agonist on the GABA receptor.

Studies report that there is no clear evidence about safety issues concerning taurine, although there are papers which describe taurine-caffeine interactions from energy drinks (Schaffer *et al.,* 2014). A recent article states that combinations of taurine, caffeine and guarana could lead to neurotoxicological effects that could disturb homeostasis. The authors of this article suggest that a combination of high depletion of ROS-mediated cellular signaling and caffeine-mediated induction of apoptosis leads to a loss of structure in cells. After the guarana treatments with caffeine and/or taurine doses, the loss of structure in the cells will lead to cell apoptosis. Figure 1 describes how those combinations could lead to health problems (Zeidán-Chuliá *et al.,* 2013).

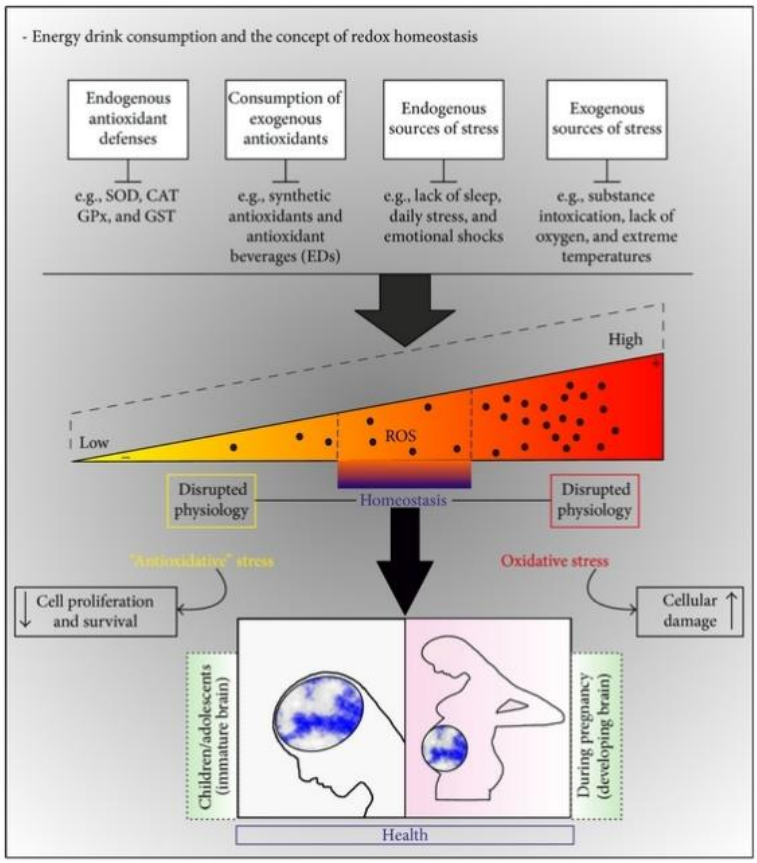

Figure 1: Schematic concept of oxidative stress and homeostasis.

An important actor in the food industry and legislation is the EFSA (European Food Safety Authority). They state in their article of 2009 that taurine is a natural body constituent and they conclude that exposure of taurine with the concentration in ED's are not of safety concern (The EFSA Journal, 2009)

2.3 Glucose

Another important ingredient of ED's is glucose ($C_6H_{12}O_6$). This is a monosaccharide that can be found in plants. After photosynthesis in plants glucose is one of their main products. In cells of many organisms including human cells, glucose is a secondary source of energy, a metabolic intermediate and is needed for cellular respiration. The largest amounts of glucose are stored in the liver and some in the muscles as glycogen. Glucose and oxygen are delivered by blood going to tissues and via diffusion reaches the cells.

To use the glucose for energy (ATP) in cells there are two ways of gaining the ATP by aerobic or anaerobic respiration, see figure 2. The two ways both start with glycolysis metabolic pathway where glucose is being phosphorylated by hexokinase, now glucose-6-phosphate. By the phosphorylation a charged phosphate group is made that the glucose cannot leave the cell easily. After this step it will be converted into pyruvate, generating 2 ATP per glucose. In the aerobic respiration pathway the pyruvate is oxidized to form HCO_3 which generates 36 ATP per glucose. Anearobic respiration will not oxidize the pyruvate but will reduce it to lactate, which is transported out of the cell.

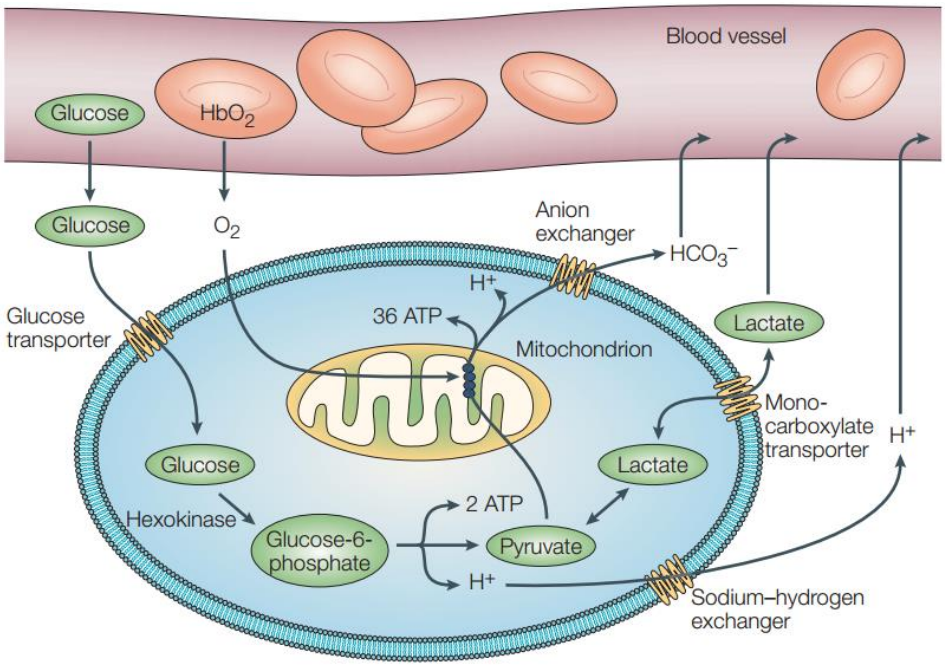

Figure 2: Schematic overview of the glucose pathway

Both pathways produce hydrogen ions (H^+) which can damage DNA, cells when in unbalance with anti-oxidants. For the majority of organisms, there is a correlation between metabolic rate and life span, but this is not the case for some animals, namely bird and primate species. Those species have a longer life span, due the fact that mitochondria produce fewer ROS (Harman *et al.*, 1957).

This indicates that reactive oxygen species (ROS) production could be a better indication of longevity than metabolic rate (Finkel *et al.,* 2000). ROS is derived from the oxidative metabolism and a number of physiological functions could result in oxidative stress, which is an imbalance of production of pro-oxidant materials and ROS. On different levels oxidative damage (OD) can be done by ROS; it could damage macromolecules, cells and tissues that increase during time in the body if the antioxidant defense and repair mechanisms are overruled. Oxidative stress can lead to accelerated ageing, by causing more vulnerability to environmental stress and pathogens eventually resulting in a decreased fitness (Rubolini *et al.,* 2012).

2.4 Miscellaneous

ED's also contain other substances than only caffeine, glucose and taurine. Some of these substances are different kinds of vitamins, like folical acid (vitamin B_9) but also herbal supplements like ginseng and guaraná which will be discussed in this paragraph.

2.4.1 Vitamins

Many ED's contain different amounts of B vitamins and their manufacturers claim that those ingredients give the body an increase in energy level, 'energy boost'. But most people have a balanced diet which will provide enough vitamin B and a higher quantity is not necessary (Williams *et al.,* 2007).

Vitamins have multiple functions in the human body. An example would be that vitamins are metabolic regulators. Thereby vitamins have influence on a number of physiological processes that are important for exercising. One of these vitamins that is influencing this process are vitamin B-complexes which help with the energy production out of fats, important for having continuous energy supply when exercising. Other vitamin B-complexes help with the formation of hemoglobin in the red blood cells, which deliver oxygen to the muscles and organs. The main function of vitamin C and E is being an antioxidant, keeping ROS in balance and therefore preventing oxidative stress from damaging the body cells (Williams *et al.,* 2004).

Although in certain cases like females whom are pregnant, additional vitamin B_{11} is recommended before and throughout pregnancy (Milunsky *et al.,* 1989). Studies of Durga *et al.* show that a 3-year folic acid treatment can improve performance tests. In older adults the speed of processing information and memory was improved. Other trials shown that additional folic acid in patients with mild cognitive impairment and dementia can have improved effects on their mental state (Durga *et al.,* 2007).

2.4.2 Herbal supplements

One of the herbal supplements is ginseng. Ginseng is used in many different products and worldwide, but the mechanisms of this herb are not well established. Some information is available like the structural different isomerism and stereoisomerism that is exhibited by the ginsenosides, the working compounds of ginseng, leads to different pharmacological effects. *In vitro* there is some evidence that ginsenosides may have effects on the plasma membrane and multi receptor systems, although *in vitro* this has never been proven (Meyer *et al.,* 2004).

However side effects of using ginseng are reported. Some side effects include high blood pressure, low blood pressure and pain in the breast (Hong *et al.,* 2002). Ginseng in combination with antidepressants could lead to a mild form of a serotonin syndrome (Fugh-Berman *et al.,* 2000).

Guaraná is another herb supplement which is one of the ingredients in ED's. The extracts of the seeds contain caffeine, saponins and tannins. The latter two can have antioxidant effects. Catechin and epicatechin, which are flavonoids and also present in guaraná, can reduce platelet aggregation (Subiah et al., 2008). Just like ginseng, there is much scientific data that prove if there are any physical or mental improvements of the ingredients of guaraná other than the caffeine content (McLellan *et a*l., 2012).

3 Brain function

If ED's would have effect on brain function, the ingredients would first have to pass the blood brain barrier. Still some studies show improved brain functions of ED's, like Wesnes et al., 2013, Heatherley et al., 1987 and Lieberman et al., 2005. Figure 3 shows the benefits of energy shots among six different tests of cognitive function. The differences of effect size are changes of the baseline between placebo and energy shots. Diverse results are found in other studies, one of those studies shows that there is a fast decrease of cerebral blood flow, after young individuals drink an ED. Therefore questions could be asked about the claim of ED manufactures on improving the mental state of consumers (Grasser *et al.,* 2014).

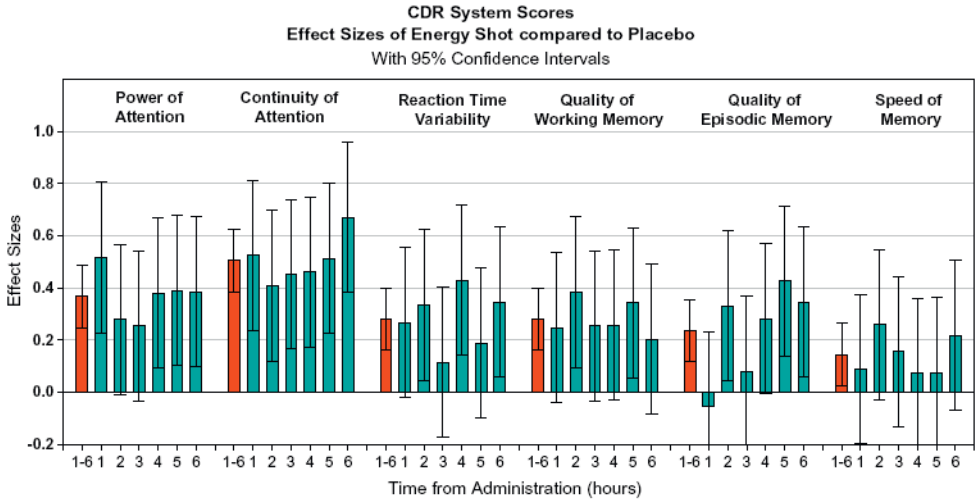

Figure 3: Differences of effect size change of the baseline between placebo and energy shots of different cognitive function tests, adapted from Wesnes *et al.,* 2013.

Caffeine

Many effects of EDs are ascribed to caffeine, also effects on brain function. High doses of 200 mg (drinking high quantities of EDs) have effects on the brain like attention, information processing and sometimes improvements of the episodic memory (Smith *et al.,* 2011). In this study the ED did not include sugar, which most ED's have.

Another study of Scholey *et al*., 2004 showed no effects on brain function of an ED with caffeine (75 mg) and sugar (37, 5). In a double-blind, a placebo-controlled, randomized trial, the same caffeine dose (75 mg) was used. The results of this study stated improvements of reaction time, vigilance, ability to focus attention, accuracy of responses, and ability to recall number sequences (Haskell *et al.,* 2005). An additional study showed an increase of accuracy and decrease of reaction time in a group of young adult men to acute intake of caffeine with dose of 64 mg (Lieberman *et al.,* 1987).

However some older studies provide evidence those high amounts of caffeine alone can have undesirable effects on the mood (Lieberman *et al.,* 2007). Those high dose (200-300 mg) effects of caffeine occur in the dopamine-mediated brain reward system mood (Nehlig *et al.,* 1986). Not only the motor system will be activated but also the sleep-wake cycle, which stimulates the increase of cerebral energy metabolism, resulting in a bad mood (Nehlig *et al.,* 1984).

Studies seem to find no effects, negative effects and positive effects whether caffeine is ingested alone or via EDs. Governments are also conducting much research on caffeine and its function. In their final report of the Institute of Medicine Food and Nutrition Board Committee on Military Nutrition Research, they note that the caffeine intake (dose 150 mg) increases brain function and the effects can last until 10 hours after intake (Institute of Medicine Food and Nutrition Board Committee, 2000).

Taurine

The ED manufactures claim that taurine also would have increasing effects on brain function. Although studies show no increase, the study of Galloway *et al*. showed that additional taurine for 7 days had no effect on muscle taurine levels and no effect on muscle metabolism during exercise. Also the blood-brain barrier is securely regulated and the taurine levels in the brain would not be changed (Galloway *et al.,* 2008*).* But on the other hand studies done in this field lack the experimental trials and cannot isolate the effect of taurine (Kang *et al.,* 2002).

Glucose

A study shows that the rate of glucose consumption and the formation rate of glutamine in the brain are equal. So the usage of glucose for brain function could be measured by the amount of glutamine formation in the brain. The study explains that the total energy expenditure on glutamatergic signaling is indeed significant. 74% of the glucose consumption is processed through glutamine pathways in humans (Sibson *et al.,* 1998).

Concluding that the intake of EDs can lead to energy boosts, which can increase the brain function. Although other studies suggests otherwise and report that the amount of glucose present in EDs would not be sufficient to have a positive effect during exercising. In contrast to sport drinks, studies report that sport drinks have a positive effect on brain function and physical activity (Sibson *et al.,* 1998). Some studies state that there are beneficial effects of the glucose in EDs for increasing the brain function up to 60 minutes after intake (Scholey *et al.,* 2004).

Vitamins

As for vitamins no experimental studies were found that could show positive or negative effects on the brain function, also not in combination with the other ingredients present in EDs (McLellan *et al*., 2012).

4 Blood pressure

To briefly recap what blood pressure (BP), is a short introduction is given below. After this the four main ingredients of ED will be described; caffeine, taurine, glucose and supplements. Although due the high interaction effects those will be discussed together. BP is pressure put forth by the blood that is circulating against the walls of the blood vessels. The BP depends on the blood pressure itself (action of the heart) and the resistance of the blood vessels. In humans an increased BP is observed with increasing age The precise cause of this rise in BP is still not fully understood.

In the literature age has a major influence on high and low BP. As in individuals older than 50 years old, high BP leads to cardiovascular diseases (CVD), causing hypertension. This causes heart failure in the end (Chobanian *et al.,* 2003). However higher BP was associated with lower mortality in people above the age of 85. In elderly, low BP seems to be associated with poor health leading to higher mortality (Boshuizen *et al.,* 1998). As indicated above age matters in terms of the effects of ED's on the BP in humans. Nevertheless most studies with the effects of ED's are done in young healthy individuals.

The study of Menci *et al.* showed that in young individuals, drinking an ED containing sugar, caffeine (0.03%), and taurine (0.4%) had a potential positive effect on the cardiac muscle contractions. Taurine alone seems to have a similar effect on the contractility of the heart by reducing the left ventricular end-diastolic pressure in patients with heart failure (Jeejeebhoy *et al.,* 2002). But the effect of caffeine on the increase of contraction in the heart muscles has not been backed up by the literature (Giacomin *et al.,* 2008; Menci *et al.,* 2013). A high dose of caffeine by itself can have negative effects on the heart, an increase in heart beat, BP and resistance of the blood vessels (Lieberman *et al.*, 2001).

BP and stress are related to each other. A couple studies confirmed this relationship (Muller *et al.,* 1989; Schnall *et al.,* 1992). The role of ED's on stress are not tested yet but as described above there are studies that point out the effects of ED's on BP. Cortisol is released and regulated by the hypothalamus due stress responses. Normally this rise in cortisol would be restrained through the negative feedback loop of cortisol at the pituitary and hypothalamus (Dallman *et al.,* 1987). When cortisol secretion stays increased, it could give rise to a decrease in immune response, leading to depression and decline in memory functions (Lupien *et al.,* 1999). Caffeine (300 mg a day) on its own could give rise to cortisol in the afternoon which could be relevant information for individuals who already have complications (Lovallo *et al.* 2005).

5 Age related diseases

To combine the knowledge of ingredients of the EDs and two diseases which are mostly present in elderly. Alzheimer's disease and type 2 diabetes will be discussed.

Alzheimer's disease

The most common form of dementia is caused by the Alzheimer's disease (AD). Mostly older people (65 years and over) are diagnosed with AD but when diagnosed the disease has already progressed through a couple of stages. Papers suggest that in 2050, almost 1 in 85 persons will be affected by AD worldwide.
One cause of AD is the aggregation of toxic proteins, mainly plaques and tangles, in the brain. For example the plaques are protein deposits of the fragment beta-amyloid (Aβ), which in aggregated form can induce neuronal cytotoxicity. Tangles are unusual structures that are formed by the tau proteins that have changed inside the nerve body cells. As the AD progresses, the nerve cells of the patient's brain will shrink and eventually die. This will results in the loss of brain functions and in brain damage which leads to dementia (Sung *et al.,* 2014).

There are multiple theories about the cause of AD. One of these theories suggests that oxidative stress would have a major impact on early development of the disease. The body has responses to the oxidative stress, induction of anti-oxidant enzymes, tau phosphorylation and NFT formation are all protective mechanisms (Su *et al.,* 2008; Kastenholz *et al.,* 2009). But when one of these mechanisms would be down regulated or an imbalance would be achieved between oxidative damage and the body's responses this could lead to Alzheimer (Pohanka *et al.,* 2013).

Energy drinks (ED), as explained before, contain high doses of caffeine, taurine, glucose (not in sugar free EDs) and anti-oxidants. Studies described earlier (also figure 3) show that, caffeine has a positive effect on cognitive functions. This increase of brain function could help patients of AD live longer with a functional brain. Unfortunately EDs will not help curing the disease of AD (Wesnes *et al.,* 2013).

The literature contains papers about taurine being an anti-oxidant, which is supported by the claims of the ED manufactures but proof of taurine being a direct scavenger of the ROS has not been found (Schaffer *et al.,* 2010). However taurine seems to have impact on the ROS generation in the mitochondria (Ito *et al.,* 2008). The high amounts of anti-oxidants (see table 1) could have positive effects on the body's response to the oxidative damage, due the scavenging of ROS by the anti-oxidants (Williams *et al.,* 2004). However this result has not been found yet, also not in combination with all the other ingredients of energy drinks.

Diabetes type 2

Another disease that occurs much in the Western society is type 2 diabetes. In Europe (and all around the world) the number of people developing type 2 diabetes is increasing. Important factors are reduction in activity, obesity and food patterns (Baan *et al.,* 2014). Men and women in Europe drink about one glass of sugar-sweetened soft drink a day. This consumption was associated with an increased Body Mass Index (BMI) and diabetes type II correlation but not significant (Romaguera *et al.,* 2013). Another study suggests that sugar-sweetened soft drinks are associated with weight gain, the development of the metabolic syndrome and type 2 diabetes (Vasanti *et al.,* 2010).

6 Discussion & conclusion

Caffeine seems to be the only correctly tested supplement of the many supplements ED. Also caffeine on its own could be held responsible for the many claimed positive effects of EDs on the consumer. An overdose of caffeine could cause the negative effects (Hering-Hanit *et al.,* 2003) and might even cause the reported deaths of EDs. Caffeine in EDs has got an effect on brain function (Lieberman *et al.,* 1987, 2001). Caffeine has no scientifically proven effect in EDs on blood pressure (BP) (Giacomin *et al.,* 2008; Menci *et al.,* 2013) but by itself has got an effect on cortisol and BP which could have a negative effect for groups that are badly responsive to caffeine (Lovallo *et al.* 2005).

Taurine seems improve the brain function but this can only be proven when taurine is tested on its own and it has not been done so it cannot be scientifically confirmed that it has a function in EDs. Knowing this it could make taurine a possible hazardously compound (Schaffer *et al.,* 2014). But to be sure whether taurine is safe or unsafe more experiments have to be done. As for now taurine in EDs, does not seem to have an effect on the brain function or BP (Jeejeebhoy *et al.,* 2002).

Already a lot is known about the function and the mechanisms of glucose on itself but not in combination with caffeine, taurine, vitamins or herbs. ED is a consumer good and first of all it has to be safe for the public. As for now no interactions of glucose in EDs are registered so governments assume it has no real negative consequences, but too much EDs leads to an increase of glucose in the body. The body has to make a lot of insulin in order to keep the glucose concentration at basal levels, when it does not type 2 diabetes could be induced. When the intake of EDs is chronic, type 2 diabetes could also be induced due the increase in weight and the development of the metabolic syndrome (Vasanti *et al.,* 2010). Suggesting that reducing the intake of EDs should be done for limiting the chance of chronic metabolic disease which could cause ageing indirectly by a higher ROS production (Finkel *et al.,* 2000).

The answer to the main question: "*What is the effect of the ingredients in energy drinks on the cerebral and heart function?"* cannot be given, because the only known and proven fact until now is the effect of caffeine on cerebral and heart function, not knowing if other supplements of EDs are also contributing to this effect. As for the two other questions, "*Could energy drinks have an effect on ageing of the consumers?"* and "*What is the impact of the contents of energy drinks on the stress response of consumers?",* speculating about the answers of the questions can be done but as like the main question no real answer can be given due the lack of good evidence of those topics.

Concluding, I would suggest that people reconsider their policy on energy drinks as they are defined at this moment. Governments could put restrictions on supplements in the EDs, if the mechanisms of the supplements are scientific proven unsafe for the general public by contain well-designed experiments. Also more research should be done on the long term effects on the brain and heart cells which are affected by the EDs. At first structural studies have to be done, including all the ingredients of the ED. Those should all be tested with the same protocol, in the same dose available in EDs and unaccompanied by other ingredients present in the EDs. After this all of the interactions of all those ingredients should be tested in the same dose available as in the EDs. For all those experiments you also need many groups, young, adolescent and old with their proper controls. Another point would be to think about where to sell the product. Since selling those beverages to people who already have a hereditary tainted background for developing diabetes type II or heart failure could be further endangered.

7 References

Baan, CA. (2014). Hoe vaak komt diabetes mellitus voor en hoeveel mensen sterven eraan? *Volksgezondheid Toekomst Verkenning, Nationaal Kompas Volksgezondheid.*

Berchtold, NC. (1998). Evolution in the conceptualization of dementia and Alzheimer's disease: Greco-Roman period to the 1960s. *Neurobiol. Aging,* 19 (3): 173–89

Boshuizen, HC. (1998). Blood pressure and mortality in elderly people aged 85 and older: community based study. *BMJ*, 316(7147):1780-4.

Chobanian, AV. (2003). The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure - The JNC 7 Report. *JAMA-JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION*, 289, 19, 2560-2572. DOI: 10.1001/jama.289.19.2560

Dallman, MF. (1987). Characterization of corticosterone feedback regulation of ACTH secretion. *Ann N Y Acad Sci*, 512:402–14.

Dunwiddie, TV. (2001). The role and regulation of adenosine in the central nervous system. *Annu Rev Neurosci,* 24:31-55.

Durga, J. (2007). Effect of 3-year folic acid supplementation on cognitive function in older adults in the FACIT trial: A randomised, double blind, controlled trial. *Lancet,* 369:208–216.

Ferré, S. An update on the mechanisms of the psychostimulant effects of caffeine. J Neurochem, 105(4):1067-79.

Fisone G. (2004). Caffeine as a psychomotor stimulant: mechanism of action. *Cell Mol Life Sci*, 61(7-8):857-72.

Fugh-Berman, A. (2000). Herb-drug interactions. *Lancet,* 355:134–138. doi: 10.1016/S0140-6736(99)06457-0.

Galloway, SDR. (2008). Seven days of oral taurine supplementation does not increase muscle taurine content or alter substrate metabolism during prolonged exercise in humans. *J Appl Physiol*, 105:643–651.

Giacomin, E. (2008). Acute effects of caffeine and cigarette smoking on ventricular long-axis function in healthy subjects. *Cardiovascular Ultrasound*, 6, 9.

Grasser, E.K. (2014). Cardio- and cerebrovascular responses to the energy drink Red Bull in young adults: a randomized cross-over study. *Eur J Nutr*, doi 10.1007/s00394-014-0661-8

Haskell, CF. (2005). Cognitive and mood improvements of caffeine in habitual consumers and habitual non-consumers of caffeine. *Psychopharmacology*, 179, 813–825

Heatherley, SV. (2005). Cognitive and psychomotor performance, mood, and pressor effects of caffeine after 4, 6 and 8 h caffeine abstinence. *Psychopharmacology*, 178 , 461–470

Hering-Hanit, R. (2003) Caffeine-induced headache in children and adolescents. *Cephalalgia,* 332-335.

Hong, B. (2002). A double-blind crossover study evaluating the efficacy of korean red ginseng in patients with erectile dysfunction: a preliminary report. *J Urol*, 168:2070–2073.

Huxtable, R.J. (1992). Physiological actions of taurine. *Physiol Rev*, 72:101–163.

Institute of Medicine Food and Nutrition Board Committee on Military Nutrition Research Doses and delivery mechanisms Institute of Medicine Food and Nutrition Board committee on military nutrition research. Caffeine for the sustainment of mental task performance. Formulations for military operations, National Academy Press, Washington, DC (2001), pp. 61–65

Ishak, W. W. (2012). Energy Drinks: Psychological Effects and Impact on Well-being and Quality of Life – A literature review. *Innov Clin Neurosci*, 9, 1, 25-34.

Ito, T. (2008). Taurinedepletion caused by knocking out the taurine transporter gene leads to a cardiomyopathy with cardiac atrophy. J Mol Cell Cardiol, 44:927-937.

Jeejeebhoy, F. (2002). Nutritional supplementation with MyoVive repletes essential cardiac myocyte nutrients and reduces left ventricular size in patients with left ventricular dysfunction. *American Heart Journal*, vol. 143, no. 6, pp. 1092–1100, 2002

Kang, Y-S. (2002). Regulation of taurine at the blood-brain barrier by tumor necrosis factor-a, taurine and hypertonicity. *J Neurochem*, 83:1188–1195.

Kastenholz, B. (2009). Plant Metal Chaperones: A Novel Perspective in Dementia Therapy. *Amyloid* 16, (2): 81–3. doi:10.1080/13506120902879392.

Lieberman, HR. (1987). The effects of caffeine and aspirin on mood and performance. *J Clin Psychopharmacol*, 7, 315–320.

Lieberman, HR. (2001). The effects of ginseng, ephedrine, and caffeine on cognitive performance, mood and energy. *Nutrition Reviews*, 59, pp. 91–102.

Lovallo, W.R. (2005). Caffeine stimulation of cortisol secretion across the waking hours in relation to caffeine intake levels. *Psychosom Med*, 67, 5, 734-9.

Lupien, SJ. (1999). Working memory is more sensitive than declarative memory to the acute effects of corticosteroids: a dose-response study in humans. *Behav Neurosci,* 113:420–30.

Menci, D. (2013). Acute Effects of an Energy Drink on Myocardial Function Assessed by Conventional Echo-Doppler Analysis and by Speckle Tracking Echocardiography on Young Healthy Subjects. *Journal of Amino Acids*, vol. 2013, 7 pages, doi:10.1155/2013/646703

Meyer, K. (2004). Psychological and cardiovascular effects of guaraná and yerba maté: A comparison with coffee. Interam *J Psychol,* 38:87–94.

Milunsky, A. (1989). Multivitamin/folic acid supplementation in early pregnancy reduces the prevalence of neural tube defects. *J Am Med Assoc*, 262:2847–2852.

Muller, JE. (1989). Circadian variation and triggers of onset of acute cardiovascular disease. *Circulation,* 79:733-743.

Nehlig, A. (1984). Effects of acute administration of caffeine on local cerebral glucose utilization in the rat. *Eur J Pharmacol*, 101, 91–100

Nehlig, A. (1986). Comparative effects of acute and chronic administration of caffeine on local cerebral glucose utilization in the conscious rat. *Eur J Pharmacol*, 129, 93–103

Pohanka, M. (2013). Alzheimer´s Disease and Oxidative Stress: A Review. *Curr. Med. Chem,* 21 (3): 356–64. doi:10.2174/09298673113206660258.

Reissig, C.J. (2009). Caffeinated energy drinks – A growing problem. *Drug and Alcohol Dependence*, 99, 1-3, pages 1-10.

Ripps, H. (2012). Review: Taurine: a "very essential" amino acid. *Mol Vis*, 18:2673-86.

Romaguera, D. (2013). Consumption of sweet beverages and type 2 diabetes incidence in European adults: results from EPIC-InterAct The InterAct consortium. *Diabetologia*, 56:1520–1530. DOI 10.1007/s00125-013-2899-8.

Rosenbloom, C. (2007). Can vitamins and mineral supplements improve sports performance? *Nutr Today*, 42:74–80.

Schaffer, S.W. (2014). Effect of taurine and potential interactions with caffeine on cardiovascular function. *Amino Acids*.

Schaffer, SW. (2010). Physiological roles of taurine in heart and muscle. Journal of Biomedical Science, 17(Suppl 1):S2.

Schnall, PL. (1992). Relation between job strain, alcohol, and ambulatory blood pressure. *Hypertension,* 19:488-494.

Scholey, AB. (2004). Cognitive and physiological effects of an “energy drink”: An evaluation of the whole drink and of glucose, caffeine and herbal flavouring fractions. *Psychopharmacology* (Berl), 76:320–330.

Sibson, NR. (1998) Stoichiometric coupling of brain glucose metabolism and glutamatergic neuronal activity. *Proc Natl Acad Sci U S A,* 95: 316−321.

Smith, AP. (2011). Caffeine practical implications. *Diet, Brain, Behavior, Practical Implications*, 271–292.

Steinke, L. (2009). Effect of ‘‘energy drink’’ consumption on hemodynamic and electrocardiographic parameters in healthy young adults. *Ann Pharmacother,* 43:596–602

Su, B. (2008). "Oxidative Stress Signaling in Alzheimer's Disease". *Curr Alzheimer Res* 5, (6): 525–32. doi:10.2174/156720508786898451.

Subbiah, MTR. (2008). Studies on the nature of anti-platelet aggregatory factors in the seeds of the Amazonian herb guarana (Paullinia cupana). *Int J Vitam Nutr Res*, 78:96–101.

Sung, SC. (2014). Alzheimer’s Disease and Stem Cell Therapy. *Exp Neurobiol*, 23 (1), 45-52.

Vasanti, SM. (2010). Sugar-Sweetened Beverages and Risk of Metabolic Syndrome and Type 2 Diabetes. *Diabetes Care*, 33, 11, 2477-2483.

Wesnes, KA. (2013). An evaluation of the cognitive and mood effects of an energy shot over a 6 h period in volunteers. A randomized, double-blind, placebocontrolled, cross-over study. *Appetite*, 67, 105–113.

Williams, MH. (2004). Dietary supplements and sports performance: Introduction and vitamins. *J Int Soc Sports Nutr,* 1:1–6.

Worthley, MI. (2010). Detrimental effects of energy drink consumption on platelet and endothelial function. *Am J Med,* 123:184–187

Zeidán-Chuliá, F. (2013). Major components of energy drinks (caffeine, taurine, and guarana) exert cytotoxic effects on human neuronal SH-SY5Y cells by decreasing reactive oxygen species production. *Oxid Med Cell Longev,* 791-795. doi: 10.1155/2013/791795.

8 Disclaimer

rijksuniversiteit groningen