# Theoretical review: Effect of caffeine intake on food consumption patterns and body weight gain.

Alumna: Noelia Monlleo Romero.

DNI: 53790598-S.

Titulación: Psicología.

Profesora: Mercé Correa Sanz.

Convocatoria: Junio

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**ABSTRACT**

This study constitutes a theoretical review about the effect of caffeine intake in humans and animals. Before explain some peculiarities about the caffeine and add some information about the impact on the organism and behaviour it has been reviewed the existing bibliography. It has been searched for the impact of the caffeine consumption in relation to the sugar metabolism in humans and to the glucose intake and weight in animals too. Moreover, it has also been searched for information about the effect of caffeine on the maternal caffeine intake and the weight of the offspring, the effect on the obesity and the effect on eating disorders such as anorexia or bulimia. Then are exposed the results obtained in different databases that is the amount of articles that have been published in relation to the topic of the review. It has been found that caffeine has an effect on glucose metabolism. Moreover, caffeine intake is related to obesity and some Eating Disorders such as Anorexia Nervosa or Bulimia Nervosa. This substance has also been associated with offspring weight, specifically, producing a weight loss in newborns. From this review, we will propose future research to deepen into some aspects.

**Keywords**: *Caffeine, Glucose Metabolism, Glucose Intake, Obesity, Anorexia, Bulimia, Weight, and Offspring*.

**RESUMEN**

Este estudio constituye una revision teórica sobre el efecto de la cafeína en humanos y en animales. Antes de explicar algunas peculiaridades de la cafeína y añadir cierta información acerca del impacto en el organismo y el comportamiento, se ha revisado la bibliografía existente. Se ha buscado el impacto del consumo de la cafeína en el metabolismo del azúcar en humanos y también al consumo de la glucosa y el peso en los animales. Además, también se ha buscado información sobre el efecto de la cafeína en la obesidad, en los trastornos alimentarios como la anorexia o la bulimia y el impacto que tiene el consumo materno en lo que se refiere al peso de la descendencia. A continuacion, se exponen los resultados obtenidos en diferentes bases de datos. Estos se han sacado de los artículos que han sido publicados en relación con el tema de la revisión. Se ha podido comprobar que la cafeína tiene un efecto en el metabolismo de la glucosa y que además su consumo está relacionado con la obesidad, así como con algunos trastornos alimentarios como la Anorexia Nerviosa y la Bulimia Nerviosa. Esta sustancia también se ha relacionado con el peso de la descendencia, concretamente, produciendo una pérdida de peso en los recién nacidos. A partir de esta revisión se propondrá una futura línea de investigación para profundizar en algunos aspectos.

**Palabas clave:** *Cafeína, Metabolismo de Glucosa, Consumo de Glucosa, Obesidad, Anorexia, Bulimia, Peso y Descendencia*.

## 1. INTRODUCTION

The major source of caffeine is coffee beans, which are the seeds of the *Coffea arabica*. Caffeine is a drug widely used in the world. In United States, for example, it's approximated that 80-90% of adults habitually drink caffeinated drinks. The average adult caffeine intake in the USA has been predicted at 200-400 mg per day. In Spain, 63% of people over 15 years of age consume at least one cup of coffee per day. The national average of coffee intake is between one and three cups per day. Around 44% of Spanish people drink between one and two coffees and 34% between two and three, without significant sex differences. People with the highest consumption of coffee are between 46 and 55 years old.

**Caffeine actions that can affect its consumption.**

Caffeine is mostly consumed for its stimulating and fatigue-reducing effects. At high doses, humans experience feelings of tension and anxiety (Meyer & Quenzer, 2005). However, in some studies, humans receiving intermediate or low doses inform of a variety of positive subjective effects (feelings of well-being, improved energy, increased alertness and concentration). Some of caffeine's subjective effects may be related to its peripheral physiological actions. These include augmented water excretion (diuresis), increased blood pressure and respiration rate. Although the influence of caffeine on blood pressure is not generally big, chronic caffeine use may represent a risk factor for heart disease (James, 2004). Although caffeine is not usually considered as a medicinal agent, it has some therapeutic uses. Thus, caffeine is effective in the treatment of headache either alone or in combination with aspirin (Meyer & Quenzer, 2005). Possibly the most important clinical use is for the treatment of newborn infants with apneic episodes (periodic cessation of breathing) (Meyer & Quenzer, 2005).

People chronically exposed to caffeine develop tolerance to al least some of caffeine's subjective effects as well as its capacity to interrupt sleep (Meyer & Quenzer, 2005), and chronic use of caffeine also produces tolerance to the cardiovascular and respiratory effects of this drug (Meyer & Quenzer, 2005). Moreover, there is a range of caffeine withdrawal symptoms, including headache, drowsiness, fatigue, impaired concentration and psychomotor performance, and in some cases mild anxiety or depression. These symptoms can appear in individuals who are consuming as little as 100 mg/day (Griffiths et al. 1990). In some individuals the positive effects of caffeine may be due to the relief of withdrawal symptoms (Meyer & Quenzer, 2005), and it has been shown that physical dependence

plays an important role in the negative reinforcing effects of caffeine and the choice to consume caffeinated beverages (Meyer & Quenzer, 2005). Caffeine withdrawal symptoms can be severe enough to produce occupational and/or social dysfunction in heavy consumers who have severe physical drug dependence. There is even evidence that some schoolchildren become dependent on caffeine due to a strong intake of cola and other drinks or food. In fact, it has been reported recently the occurrence of frequent headaches in children and adolescents who were consuming at least 1.5 litres of cola drinks (containing about 200 mg of caffeine) per day (Meyer & Quenzer, 2005).

It's important to distinguish between the effects of caffeine consumed at normal levels and other effects observed with high amounts or in sensitive consumers. On the one hand, we find several studies which have shown beneficial effects of caffeine on simple reaction time (Clubley et al. 1979) and choice reaction time (Smith et al., 1977; Lieberman et al. 1987; Roache & Griffiths, 1987). Smith et al. (1999) and Smith (2001) have shown that caffeine increases the speed of processing new stimuli. Lorist and Snel (1997) have also shown that target identification and response preparation are improved by caffeine, and Ruijter et al. (1999) have manifested that the amount of information processed is greater after the intake of caffeine. In the same way, when performance of reaction time tasks was measured before and after a normal working day, caffeine consumption during the day decreased the slowing of reaction time seen at the end of the day, suggesting that caffeine may keep performance levels at work (Brice & Smith, 2001). On the other hand, Regina et al. (1974) studied the effects of caffeine on a simulated driving task. The results indicated profitable effects of this substance and confirmed findings using laboratory vigilance tasks. Moreover early studies showed that caffeine intake may have beneficial effects which could improve safety not only in automobile driving, but also other transport operations and industry (Lieberman, 1992). Moreover, Lieberman (1992) said: "When caffeine is consumed in the range of doses found in food, it improves the ability of consumers to execute required tasks sustained attention, including simulated automobile driving. Furthermore, when administered in the same dose range, caffeine increases self-reported alertness and decreases sleepiness". In this way, coffee can eliminate the decreased alertness generated by consumption of a meal (Smith et al. 1991; Smith & Phillips, 1993). Additionally, alertness is occasionally reduced by minor illnesses such as a common cold, and researches have shown that caffeine can eliminate the impaired performance and negative mood associated with these illnesses (Smith et al. 1997). The performance on an easy letter cancellation task was enhanced as caffeine dose increased (Smith, 2002). Nevertheless, there are some results that do not fit this pattern and could reflect other individual differences such as expectancies or caffeine use.

Another feature of caffeine is that it can reduce sleepiness and it can interfere with normal sleep. A number of researches have shown that caffeine increases sleep latency, many times in the first half of the night (Zwyghuizen-Doorenbos et al. 1990), and reduces the sleep duration (Hicks et al. 1983). Individuals normally control their caffeine intake to avoid interference with sleep. There are many individual differences in the effects of caffeine on sleep. For example, one study has demonstrated that caffeine given even in the early morning can affect the subsequent night's sleep (Landolt et al. 1995), while other individuals inform that they can consume caffeine before bedtime with no impact on their sleep (Colton et al. 1967; Levy & Zylber-Katz, 1983). There are possibly several reasons for these differences, but it appears to be established that high consumers appear less likely to inform sleep disturbance than those who consume it infrequently (Snyder & Sklar, 1984).

**Relationship between caffeine intake and sugar intake or metabolism**

Caffeine acutely increases blood glucose and decreases insulin sensitivity (Lane et al. 2004; Krebs et al. 2012; Egawa et al. 2009; Moisey et al. 2008). Long-term consumption has positive metabolic effects, such as increased secretion from adipocyte of adiponectin, a hormone with insulin sensitizing qualities (Fisman & Tenenbaum, 2014). Coffee it's composed of a mixture of substances such as chlorogenic acid (GCA), melanoidins, quinides and N-methylpyridinium (NMP). These have clearly shown the potencial to impact on glucose and insulin metabolism (Palatini, 2015; Tagliazucchi & Bellesia, 2015; Fu et al. 2015; Riedel et al. 2014; Li et al. 2014; Boettler et al. 2011; Shearer et al., 2003) because they have antioxidant and/or glucose metabolism regulating properties whose levels are influenced by the roasting processes (Natella & Scaccini, 2012). In animal models, it has been shown that caffeine affects glucose intake and weight. For example, Susan et al. (2010) informed that rats given a diary supplement to their maintenance diet that included a non-energetic sweetener ate more and consequently gained weight. However, rats given drinks sweetened with saccharin gained considerably more weight than rats given solutions sweetened with glucose. The addition of caffeine can provoke increased consumption of diet drinks, and could exacerbate the increases in energy intake and body weight gain related with increase consumption of non-caloric sweeteners. Additionally, caffeine has been associated to decreased body weight (Swithers, Martin, Clark, Laboy & Davidson, 2010).

**Caffeine intake and obesity**

Caffeine intake has also been associated with obesity. Obesity is a chronic disease caused partially by the dietary habit of consuming excessive nutrients, especially those with high-fat content. This may be defined as accumulation of fat to an extent that the health of the individual is impaired (Leong & Wilding, 1999). Prevalence of obesity continues to increase worldwide, mainly as a result of changing lifestyles. Environmental factors including diet that impact internal hormonal balance and normal brain functions leading to excessive energy consumption have been recognized as relevant contributing causes of the worldwide obesity epidemic (Newbold, Padilla-Banks, Jefferson & Heindel, 2008; Wells & Siervo, 2011; Taubes, 2012; Thayer, Heindel, Bucher & Gallo, 2012; Heindel, 2003).

However, moderate consumption of caffeine inhibits fat accumulation and stimulates lipid metabolism in the liver (Kobayahi-Hattori, Mogi, Matsumoto & Takita, 2015; Sugiura et al. 2012). Tools for obesity management (caffeine or ephedrine) have been proposed as strategies for weight loss and weight maintenance, since they may increase Energy Expenditure (EE) and have been proposed to counteract the decrease in metabolic rate that is present during weight loss. Caffeine as a thermogenic agent has been investigated for potential use in body weight reduction. A possible mechanism by which caffeine affects thermogenesis involves inhibiting the phosphodiesterase-induced degradation of intracellular cyclic AMP (cAMP) (Dulloo, 1993). Hepatic thermogenic processes triggered by lactate and the formation of triglyceride after hepatic reesterfication may explain the thermogenic contribution to the effect of caffeine (Astrup et al. 1990).

The stimulatory effect of caffeine on thermogenesis in man is well established (Acheson, Zahorska-Markiewics, Pittet, Anantharaman & Jequier, 1980; Astrup et al. 1990; Bracco, Ferrarra, Arnaud, Jequier & Schutz, 1995; Dulloo, Geissler, Horton, Collins & Miller, 1989; Hollands, Arch, Phil & Cawthorne, 1981). Reduced food intake after caffeine consumption has been shown as well (Racotta, Leblanc & Richard, 1994; Tremblay, Masson, Leduc, Houde & Despres, 1988). Thus caffeine can influence both EE and energy intake.

It has been shown that combining food ingredients involved in lipid metabolism is useful for the prevention or treatment of obesity. For example, the thermogenic effect of ephedrine can be markedly potentiated by methylxanthines, such as caffeine. Indeed, nonhuman animal studies showed that the effect after an ephedrine/caffeine mixture was larger than that with ephedrine or caffeine alone (Dulloo & Miller, 1987; Dulloo & Miller, 1986; Ramsey, Colman, Swick & Kemnitz, 1998; Tulp &

Buck, 1986). In a long-term study (6 moths) of 167 obese subjects, the ephedrine/ caffeine mixture group lost significantly more weight than the placebo group (Boozer et al. 2002). Furthermore, a mixture of thiamine, L-arginine, caffeine, and citric acid has been shown to have an anti-obesity effect in obese mice and humans with a high Body Mass Index (BMI) (Muroyama et al. 2003; Muroyama, Murosaki, Yamamoto, Ishijima & Toh, 2003). It has been shown that a combination of G-hesperidin and caffeine reduces accumulation of body fat via inhibition of hepatic lipogenesis, whereas G-hesperidin or caffeine alone show little effect (Ohara, Muroyama, Yamamoto & Murosaki, 2015). Glucosyl hesperidin (G-hesperidin) has been reported to reduce serum levels of triglyceride (TG) in animals (Akiyama et al. 2009; Chiba et al. 2003; Mitsuzumi, Arai, Sadakiyo & Kubota, 2011) and subjects with hypertriglyceridemia (Miwa et al. 2004; Miwa et al. 2005).

Kamimori, Somani, Knowlton & Perkins (1987), proposed that obesity, exercise, and a combination of exercise and obesity could affect the pharmacokinetics of caffeine. This substance is a highly lipophilic drug. Fat is virtually water-free tissue and dosing regimens based on total body weight would result in much higher serum drug concentrations in individuals with greater amounts of fat.

**Caffeine intake and Eating Disorders.**

Eating Disorders has also been associated with caffeine intake. The rates of co-morbid Eating Disorders (EDs) and Substance Use Disorders (SUDs) reported in the literature are high. Studies have reported that up to 50% of patients with an eating disorder will abuse alcohol or an illicit substance, compared with 9% of the general population (National Ctr on Addiction and Substance Abuse at Columbia University, 2003) although in a more recent review of the literature, rates of between 17% and 46% were reported (Harrop & Marlatt, 2010).

Traditionally, Bulimia Nervosa (BN) has had the strongest reported association with substance use compared with Anorexia Nervosa (AN) (Glasner-Edwards et al. 2011; Krug et al. 2009; Root et al. 2010). In a meta- analysis of the literature, Calero-Elvira et al. (2009) reported the highest prevalence of substance use in those with BN purging type followed by those with Binge Eating Disorder (BED), compared with the healthy population, whereas those with AN restricting type had lower levels of drug use than healthy controls. However, some recent studies have documented that co-morbid AN and SUDs may be more prevalent than previously thought, particularly for those with AN with bulimic features (Krug et al. 2009; Root et al. 2010; Baker et al. 2010). Baker et al. (2010) reported in their study that caffeine and tobacco were the most frequently used substances, and women with AN were more likely to have a caffeine disorder (26%), compared with those with BN (23%).

However, this difference was found to be non-significant.

Individuals with EDs seem to have a tendency to consume high amounts caffeine through energy drinks, coffee and/or caffeine pills to increase energy levels and suppress appetitive (Hart, Abraham, Luscombe & Russell, 2005). Patients with AN or BN consume caffeinated beverages excessively to stimulate their energy without the unwanted effect of consuming calories.

Beverages such as diet energy drinks, coffee and tea often contain caffeine and artificial sweeteners. The medical repercussions of the misuse of these substances can be significant. Caffeine overuse can lead to anxiety and tremor and discontinuation can result in withdrawal symptoms including headache and concentration difficulties (American Psychiatric Association, 2000). In combination with these medical problems, compensatory behaviours (e.g., vomiting or laxative abuse) may produce more adverse medical sequelae. In addition, patients with AN have impaired osmoregulation and difficulty concentrating urine when dehydrated (Everard, Pinto de Cunha, Lambert & Devuyst, 2004).

Caffeine use may vary over the course of an eating disorder. Striegel-Moore et al. (2006) observed that caffeine intake increased sharply in individuals with AN after they were first diagnosed and decreased subsequently. More specifically, intake of coffee or tea increased after AN onset, but intake of chocolate food (containing caffeine) decreased. Some research has suggested that participants with BN do not show increased caffeine consumption when compared with participants with AN. Others studies suggest that patients with BN or anorexia nervosa-binge-purge (AN-B/P) who binge eat and purge show increased caffeine consumption compared with patients with anorexia nervosa-restricting subtype (AN-R). Additionally, Stock et al. (2002) observed patients with AN-B/P or BN with purging behaviour overused caffeine (three or more caffeinated drinks per day), compared with patients with AN-R. Although the exact cause of increase caffeine consumption is unknown, consuming excessive amounts of caffeine containing fluids may serve as a weight control method to mask hunger, to aid in purging behaviour, or increase energy levels (Hart et al. 2005).
Reasons suggested for drinking in eating disorder patients include to: aid vomiting (Gendall, Sullivan, Joyce, Carter, & Bulik, 1997); facilitate post-vomiting irrigation, as a calorie-free alternative to food, (i.e. to falsify weight), to feel good (Salkovskis, Jones, & Kucyj, 1987); to help weight loss (Kornreich, Dan, Verbanck, Fontaine, & Pelc, 1998); to attempt to purify the body and eliminate toxins and calories via urine (Santonastaso, Sala, & Favaro, 1998). It has also been reported that patients with binge eating and purging behaviours drink excessive quantities of caffeinated beverages (Fahy & Treasure, 1991; Sours, 1983) to suppress appetite (Fahy & Treasure, 1991; Rock & Yager,

1987; Salkovskis et al., 1987), boost energy levels without consuming calories (Sours, 1983), restore energy, eliminate hunger and relieve fatigue (Salkovskis et al., 1987), control weight, increase effects of laxatives, increase metabolic rate and for its diuretic effect (Fahy & Treasure, 1991).

Patients who have objective binge eating and purging behaviours, drink to aid their vomiting behaviour and to replace fluid that is lost during purging. Patients report that when binge eating they have large quantities of fluid to make it easier to regurgitate stomach contents. Caffeinated beverages appear to be used by eating disorder patients to feel full and suppress appetite, to aid with purging, to boost energy levels and to stimulate metabolism and there is evidence that caffeine may boost energy levels, suppress appetite, and affect metabolism. AN patients were more likely to drink to 'prevent abdominal bloating' and 'aid gut transit of food' than other diagnostic groups. This motivation to drink may be associated with refeeding, due to delayed gastric emptying prior to renutrition. In this way, an eating disorder needs to be considered a disorder of fluid intake as well as of food intake.

In these cases, psychoeducation should be provided on: not drinking as a method of reducing appetite, avoiding drinking when hungry as an alternative to eating or 'to have something to do', and how eating disorder behaviours may affect fluid requirements. Clinicians should be aware that patients who have excessive caffeine intake may be likely to be engaging in binge eating and vomiting.

**Caffeine intake and its repercussion on offspring weight**

Emerging evidence has revealed that the most critical exposure window for the impact of exogenous factors (dietary or environmental) is in utero, which exerts amplifying and long-lasting effects on health outcomes in childhood and adulthood through adverse fetal programming (Newbold, Padilla-Banks, Jefferson & Heindel, 2008; Whyatt et al. 2012; Kim et al. 2011; Luo, Xiao & Nuyt, 2010; Sullivan & Grove, 2010; Heerwagen, Miller, Barbour & Friedman, 2010; Leduc, Levy, Bouity-Voubou & Delvin, 2010). One such chemical, which developing fetuses are widely exposed to, is caffeine through maternal consumption during pregnancy. In the USA, 475% of pregnant women reported intake of caffeine-containing products (Weng, Odouli & Li, 2008). In human studies, in-utero caffeine exposure has been associated with increased risk of abnormal fetal growth including small-for-gestational-age (Klebanoff, Levine, Clemens & Wilkins, 2002; Infante-Rivard, 2007; Sengpiel et al. 2013; Bakker et al. 2010; Vik, Bakketeig, Trygg, Lund-Larsen & Jacobsen, 2003; Fortier, Marcoux & Beaulac-Baillargeon, 1993). This has been associated with higher risk of obesity and metabolic syndrome after birth. Globally, it has been estimated that 15.5% of all infants are LBW. This is associated with neonatal mortality and morbidity also with a higher risk of chronic diseases

such as type 2 diabetes and cardiovascular diseases in adult life.

Pregnant women have slower caffeine metabolism, with 1.5 to 3.5 times longer half-life needed to eliminate caffeine. This substance has been detected in the amniotic fluid, umbilical cord, urine and plasma of fetuses, which suggests that it is easy transmitted across the placenta. The exposure can also lead to vasoconstriction in the uteroplacental circulation, which may in turn affect fetal growth and development (Chen, Wu, Neelakantan, Foong-Fong, Pan & van Dam, 2014). That's why the possible association of maternal caffeine consumption to a variety of pregnancy outcomes such as Low Birth Weight (LBW) is important because of widespread exposure to this methylxantine in children whose mothers regularly consume coffee.

The immaturity of a fetus liver produces a low level of enzymes necessary for caffeine metabolism, and it leaves neonates at risk of LBW (defined as a birth weight smaller than 2.500g). The cytochrome P450 1A2 enzyme (CYP1A2) predominantly metabolizes caffeine. Since the levels of CYP1A2 are believed to be low in the placenta and fetus, the fetus can be exposed to caffeine for a long period of time. Some pharmacological effects of caffeine related to fetal growth are blockade of adenosine receptors and inhibition of cyclic nucleotide phosphodiesterase (PDE). When caffeine acts as an antagonist of adenosine receptors, adenosine is unable to regulate the local blood flow during hipoxia. The acute maternal hipoxia can negatively impact the fetal cardiovascular functionand fetal growth. Also, when PDE is inhibited by caffeine, the levels of cyclic adenosine monophosphate (cAMP) will be increased because PDE degrades cAMP, which may interfere with fetal growth (Rhe et al. 2015).

## 2. METHODS

With the objective of find the necessary information, this has been consulted in some recognised databases such as PubMed, Web of Science and PsycNet and Google academic specially the first and the second one. Furthermore, it has been used an English book "Psychopharmacology, drugs, the brain and behaviour". PubMed and Web of Science are the two most used databases.

PubMed is a service of the US National Library of Medicine that adds new citations daily and provides free access to MEDLINE®, the NLM®, database of indexed citations and abstracts to medical, nursing, dental, veterinary, health care, and preclinical sciences journal articles. Moreover, includes additional selected life sciences journals not in MEDLINE.

Web of Science is an online subscription based scientific citation indexing service that provides a comprehensive citation search. It gives access to multiple databases using a variety of powerful search and analysis tools.

Psycnet is the only search platform designed specifically to deliver APA content. This is developed and engineered by APA, this powerful platform uniquely integrates the *Thesaurus of Psychological Terms*® so users can discover vital research content with ease and unrivalled precision.

The keywords used to look for the articles are: *Caffeine, Glucose Metabolism, Glucose Intake, Weight, Offspring, Obesity, Anorexia and Bulimia*.

All the information has been searched in English except for some information about the percentage of the caffeine intake in Spain.

Although it has been made several searches with all the keywords previously mentioned, the main keywords utilised are caffeine and glucose. Caffeine because it has always been related to the other words and glucose because there was more difficult to find the specific information. Normally, it has been used "and" to relate the words to each other.

In PubMed it has been chosen "Summary" and "Most recent" to find the articles. Then I read the abstract of the articles, specially the purpose, the results and conclusions. In Web of Science it has been chosen "Basic Search" and "Title" in "All Databases" to find the items and I chose that they were sort by "Publication Date-newest to oldest". In PsycNet it has been selected "Easy Search" to find information. I put the keywords in the "Look for" part and I chose that they were sort by "Year". Finally, in Google Academic I put two or three keywords in the internet browser. Normally I checked if the keywords were in the tittle of the articles and then I read the abstract and checked the keywords again.

## 3. RESULTS

In this section, I'm going to explain the number of results found after the search in the databases named in the previous section.

First, in PubMed when I wrote *Caffeine and Glucose Metabolism* I found 848 items in 43 pages. When I searched for *Caffeine and Glucose Metabolism Animals* I got 32 results in 2 pages. When I put *Caffeine and Weight Animals* I obtained 855 articles in 43 pages. When I wrote *Caffeine Intake and Offspring Weight* I found 25 items in 2 pages. When I searched for *Caffeine Intake and Obesity* I got 171 items in 9 pages. When I put *Caffeine Intake and Anorexia* I obtained only 10 items in 1 page, however, when I put only *Caffeine Anorexia* I found 28 articles in 2 pages. Finally, when I searched for *Caffeine Intake and Bulimia* I got only 7 items in 1 page, nevertheless, when I changed the search and I wrote Caf*feine Bulimia* I obtained 19 articles in 1 page too.

Secondly, In Web of Science when I wrote *Caffeine and Glucose Metabolism* I got 1.348 items in 135 pages. When I put *Caffeine and Glucose Metabolism Animals* I obtained 1.146 results in 115 pages. When I searched for *Caffeine and Weight Animals* I found 2.437 articles in a total of 244 pages. When I put *Caffeine Intake and Offspring Weight* I got 45 items in 5 pages. When I wrote *Caffeine Intake and Obesity* I got 438 articles in 44 pages. When the search was *Caffeine Intake and Anorexia* I just got 25 items in 3 pages. Ultimately, when I search for *Caffeine Intake and Bulimia* I obtained 15 items in 2 pages.

Thirdly, in PsycNet when I put *Caffeine and Glucose Metabolism* I found only 13 items. When I searched for *Caffeine and Glucose Metabolism Animals* I got 23 articles. When I searched for *Caffeine and Weight Animals* I obtained 14 results. When the search was *Caffeine Intake and Offspring Weight* I found 57 items in a total of 3 pages. However, when I wrote *Caffeine Intake and Obesity* I obtained 24 results. When I wrote Caffeine Intake and Anorexia I just got 10 items, similarly, when I Out Caffeine Intake and Bulimia I found 8 results.

Finally, when I used Google Academic and I put *Caffeine and Glucose Metabolism* I found 104.000 results in 0,19 seconds. When I wrote Caffeine and *Glucose Metabolism Animals* I obtained 51.200 items in 0,12 seconds. When I searched for *Caffeine and Weight Animals* I got 56.900 articles in 0,14 seconds. When I wrote *Caffeine Intake and Offspring Weight* I found 15.600 items in 0,15 seconds. When I searched for *Caffeine Intake and Obesity* I got 46.600 articles in 0.09 seconds. When I wrote *Caffeine Intake and Anorexia* I obtained 18.900 results in 0.08 seconds. At last, when I put *Caffeine Intake and Bulimia* I got 13.300 in 0.09 seconds.

| Search name | PubMed | Web of Science | PsycNet | Google Academic |
|---|---|---|---|---|
| **Caffeine and Glucose Metabolism** | 848 | 1.348 | 13 | 104.000 |
| **Caffeine and Glucose Metabolism Animals** | 32 | 1.146 | 23 | 51.200 |
| **Caffeine and Weight Animals** | 855 | 2.437 | 14 | 56.900 |
| **Caffeine Intake and Offspring Weight** | 25 | 45 | 57 | 15.600 |
| **Caffeine Intake and Obesity** | 171 | 438 | 24 | 46.600 |
| **Caffeine Intake and Anorexia** | 10 | 25 | 10 | 18.900 |
| **Caffeine Intake and Bulimia** | 7 | 15 | 8 | 13.300 |
| **Total** | 1.948 | 5.454 | 149 | 306.500 |

Although it seems that there is a huge quantity of articles (314. 051), many of them are the same in different databases. Nevertheless, it has been chosen those with an interesting abstract related to the different topics.

## 4. DISCUSION & CONCLUSION

The present work is a review focused on the role of the caffeine on consumatory behaviours and physiological actions on body weight gain using specially human studies.

In relation to the search results in the databases, it's interesting to give importance to the amount of articles found in different webs. On the one hand, the two searches with most results in PubMed, Web of Science and Google Academic are *Caffeine and Weight Animals as well as Caffeine and Glucose Metabolism respectively*. However, in PsycNet the two searches with most results (although not many) are *Caffeine Intake and Offspring Weight* and *Caffeine and Weight Animals*, respectively. On the other hand, the two searches with less results in PubMed, Web of Science and PsycNet are

*Caffeine Intake and Bulimia* as well as *Caffeine Intake and Anorexia*, respectively. Nevertheless, in Google Academic, the two searches with less results are *Caffeine Intake and Bulimia* and *Caffeine Intake and Offspring Weight*. This may be due because the most part of the articles related to these different topics is relatively recent and there aren't enough studies yet. For example, although I found some articles about EDs written in 2006, the most part of the literature has appeared a few years ago (2009, 2010…).

We are going to focus on the most significant articles in each section.

In the first place, we are going to explain some results about the effect of the caffeine in the glucose metabolism. It has been demonstrated that caffeinated coffee was more adverse for glucose homeostasis in comparison with decaffeinated coffee in people who were simultaneously sleep deprived (Rasaei, Talib, Noor, Karandish & Karim, 2016).

Di Girolamo et al. (2016) in the the discussion of his study suggested that the intensity changes in roasting may alter the glucoregulatory and antioxidant effects of coffee. In fact, there is a strong association between dark roasted coffee (DRC) consumption and improved post-load glucose metabolism. For it's part, green beans and light roasted coffee (LRC) have an elevated content of CGA and this enhance insulin sensitivity and secretion as well as glucose uptake. The concentration of CGA decreases with roasting, however, that of quinides, NMP and melanoidins increases (Del Pino-García et al. 2012). These changes can influence the antioxidant capacity of the coffee.
Evidences in animal models showed that quinides and NMP straightly influence glucose metabolism (Riedel et al. 2014; Shearer et al. 2003).
In the West countries, coffee-consumption accounts for a relevant part of daily antioxidant intake (Natella & Scaccini, 2012), nevertheless other factors such as physical exercise, nutrition and energy balance can influence glucose metabolism and oxidative stress.
Summarizing, DRC, as compared to LRC, both derivative from naturally-low caffeine *Laurina* coffee, manifested positive effects on glucose metabolism.

In the same way, the findings in another study indicate that habitual coffee consumption alter post-load rather than fasting glucose metabolism (van Dam et al. 2004).

In the second place, we are going to show the results about the effect of caffeine in animals, specially in rats. Swithers, Martin, Clark, Laboy & Davidson (2010) demonstrated that diary consumption of a drink sweetened with saccharin stimulated greater total caloric intake and increased body weight gain

in comparison with consuming a solution sweetened with glucose. Adding caffeine to the solutions stimulated the consumption of the drinks by rats (compared to when these were given without caffeine). Consuming the saccharin drink was accompanied by greater weight gain compared to consuming glucose solution, regardless of whether these drinks contained caffeine too. These results suggest that caffeine didn't avoid the detrimental effects of weakening the normal sweet-taste-calorie relationship; rats given saccharin and caffeine didn't gain more weight than rats given glucose and caffeine. The caffeine can stimulate behavioural activity, and can contribute to increased energy and decreased overall body weight gain (Haldi, Wynn, & Ensor, 1947). Even when the diets are high in energy, caffeine can reduce negative consequences of consuming sweetened beverages on body composition.

In a previous study (Glatzmaier & Roberts, 1995), demonstrated that leptin increase glucose metabolism in mice. Leptin is an adipocyte hormone that acts as an afferent signal in a negative feedback loop regulating body weight, and acts by interacting with a receptor in the hypothalamus (Tartaglia et al. 1995; Lee et al. 1996). A five-hour intravenous infusion of leptin into wild-type mice increased glucose turnover and glucose uptake, but decreased hepatic glycogen content. Leptin causes a complex metabolic response with effects on glucose. The findings suggest that the efferent signals from the Central Nervous System (CNS) that modulate glucose metabolism are activated by leptin. Moreover, several studies have showed that CNS, particularly hypothalamus, can regulate glucose metabolism (Miles, Yamatani, Lickley & Vranic, 1991; Leong & Clark, 1984; Lautala & Martin, 1981; Nagai, Fujii, Inoue, Takamura & Nakagawa, 1988). In conclusion, this study suggest that leptin causes a state of negative energy balance and increases metabolism of fat and glucose.

In the third place, regarding to the effect of caffeine intake on obesity, there is a study which after controlling for children's age at each weight measurement, gender, maternal age at delivery, maternal smoking during pregnancy, prepregnancy BMI and race/ethnicity, compared with no caffeine intake, maternal caffeine intake overall was associated with 87% increased risk of obesity in their offspring. Maternal caffeine intake $\geqslant$ 150 mg per day during pregnancy (high-dose group) was associated with a more than twice the risk of childhood obesity, while daily caffeine intake o 150 mg per day (low-dose group) was associated with 77% increased risk of childhood obesity (Li, Ferber & Odouli, 2014).

The results in the study of Ohara et al. (2016) showed that intake of a combination of 500 mg G-hesperidin and 75 mg caffeine for 12 weeks significantly reduced abdominal fat (especially subcutaneous fat), body weight and the BMI in subjects with a moderately high BMI. Therefore, a combination of G- hesperidin and caffeine may be useful for the prevention or treatment of obesity.

Furthermore, Li, Ferber & Odouli (2014) showed that maternal caffeine consumtion during pregnancy was associated with an 87% increased risk of childhood obesity in offspring compared with no maternal caffeine intake during pregnancy.

In the fourth place, we are going to explain the results obtained in the search of *Caffeine Intake and Anorexia* or *Caffeine Intake and Bulimia*.

Data from one study support previous evidence in literature that a high percentage of ED patients normally use caffeine with an average intake similar to that of the general population, nevertheless with a kind of binge attitude. In fact, when considering caffeine abuse and average intake during periods of heavy assumptions, ED patients show a significantly higher prevalence than healthy controls, with an excess especially among purging subtypes (Burgalassi et al. 2009).

However, Hart et al. (2005) didn't find differences between fluid intake in EDs patients with and without purging behaviour. Marino et al. (2009) found that the results of their study were not consistent with previous research that suggested participants with EDs who binge eat and purge tend to consume more caffeine. Their findings demonstrate that overconsumption of caffeine may not be for the objective of increasing energy as was hypothesized by previous authors.

The results are contradictory, so future investigation could explore the role of caffeine in eating disorder symptomatology by asking specifically whether caffeine is used to decrease appetite, boost energy, or for other reasons. Furthermore, in previous studies of caffeine intake was based only on consumption of foods and beverages, leaving for future investigations the question of whether medications containing caffeine might represent an important source of caffeine intake in EDs.

Finally, we are going to mention some results in humans about the effect of caffeine intake in offspring weight. First, we found a meta-analysis of twelve studies detected an overall 37.8% increase in the odds of LBW among women in the highest caffeine intake group in comparison with those in the lowest group. Furthermore, a dose-response analysis based on ten studies found a 3.0% increase in the odds of LBW for every 100mg of caffeine consumed per day (one cup of coffee or two cups of tea) during pregnancy (Rhee et al. 2015).

In the same way, there is a paper which conclusions are that there is a little but significant increase in the risk for LBW in pregnant women consuming more than 150 mg of caffeine per day (Fernandes et al. 1998).

Similarly, Voerman et al. (2016) have shown that children whose mothers consumed at least 6 units

of caffeine per day used to have a lower weight at birth in comparison with children whose mothers consumed less than 2 units per day.

In one study Chen et al. (2014) showed that low caffeine consumption (50 to 149 mg/day) was associated with a 13%, moderate caffeine intake (150 to 349 mg/day) with a 38%, and heavy caffeine consumption (≥350 mg/day) with a 60% higher risk of LBW as compared with very low or no caffeine intake. Furthermore, this authors indicated that for each 100 mg/ay, there was a 13% higher risk of LBW.

Finally, there is an article which authors reported a 21-28g decrease in birth weight for each additional 100 mg of caffeine consumed per day (Sengpiel et al 2013).

Further studies are needed to assess whether maternal caffeine intake during pregnancy affects long-term offspring health outcomes, as well as the causality and underlying mechanisms.

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