

# Chapter 11

## Coffee Health Effects from Early Fetal Development Through Childhood and Adolescence

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**Abstract** Coffee is a complex mixture of bioactive compounds and the major source of caffeine in the adult diet. Caffeine is a psychoactive stimulant, which is widely used by adults and increasingly adopted by the youth in the form of coffee, sodas and energy drinks. Caffeine is a legal drug that is still the object and focus of research on possible toxic and teratogenic effects on human health. As a consequence, coffee consumption during pregnancy, possible effects on the fetus and early and later ages of human development, such as childhood and adolescence, are important areas of translational toxicology to be investigated and better understood. This chapter is a tentative effort to review the most important data over the last 20 years on coffee effects, in particular, about its caffeine content, in terms of what is available regarding harmful or beneficial effects of drinking coffee regularly during pregnancy and its possible consequences to the fetus, neonate, infant and adolescent. The great majority of the studies found were epidemiological studies where the frequency of coffee consumption was self-reported by a questionnaire. Some valuable animal studies are also included as well as human studies with healthy volunteers. Overall, the take home message is that coffee consumed in moderation, 3–4 cups a day in adults and 1–2 cups a day during pregnancy is safe for human health.

**Keywords** Coffee • Effects • Fetus • Child • Adolescence

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## 11.1 Introduction

More than one billion people start their day by drinking a cup of coffee, making it the most popular drink worldwide. After oil, the coffee industry is second in the world economy (Santos and Lima 2007). Despite 20 years of reassuring research, many people still avoid coffee because they worry about its health effects, but those concerns are understandable (Medical 2004). Older studies had linked coffee drinking to a wide range of health problems from teeth discoloration (Kumar et al. 2012) to pancreatic cancer and heart disease (Medical 2004); from neural tube defects (Yoon et al. 2001) to risk of pre-term birth (Brent et al. 2011) and child hood acute leukemia (Cheng et al. 2014) to sleepiness and tiredness from caffeinated beverages in adolescents (Orbeta et al. 2006). Many of those studies focused on the caffeine content of coffee, since caffeine is a CNS stimulant known to produce harmful health effects when ingested in high concentrations (Lean and Crozier 2012).

Coffee is not only caffeine. Coffee is a complex mixture of bioactive compounds that actually can affect health positively such as, antioxidants (polyphenols), minerals (high content of potassium, low content of sodium, high content of iron and calcium) and vitamins (niacin) (Santos and Lima 1989). This chapter is devoted to the compilation of the most recent data on the effects of coffee on human development from the fetus to adolescence. It will be divided according to age ranges that share developmental and social characteristics that pose specific health related issues. The effects of coffee will be presented divided in 3 developmental periods: (a) coffee effects on the fetus and pregnant women; (b) coffee effects in infancy and early childhood; and (c) coffee effects in adolescence.

It is necessary to make a comment on how the effects of coffee were searched in the medical literature for the preparation of this chapter. Caffeine still remains as the main concern in terms of toxicity in children. Therefore, considering that coffee is the major source of caffeine in the American and worldwide diet, most of what is stated in this chapter was collected from studies on caffeine effects, as long as coffee was mentioned as part of the diet being studied.

## 11.2 Coffee Effects on the Fetus and Pregnant Women

Over the last 30 years, an enormous number of research papers were published on coffee consumption during pregnancy and possible risks for the pregnant woman and the unborn child. The association of cigarette smoking and coffee drinking habit is very common and many times a confounding factor, which most of the older studies did not take into account and led to controversial results. The majority of the studies utilized epidemiological or animal studies dealing with congenital malformations, miscarriage, pre-term birth or growth retardation. We will present a representative sample of those studies.

## ***11.2.1 Coffee and Congenital Malformations***

### **11.2.1.1 Orofacial Clefts**

A study from the National Center on Birth Defects and Developmental Disabilities NCBD, Centers for Disease Control and Prevention, Atlanta, Georgia in collaboration with New York State Department of Health and Oak Ridge Institute for Science and Education, Tennessee (Collier et al. 2009) included 1531 infants with cleft lip with or without cleft palate (CL/P) and 813 with cleft palate only (CPO) and 5711 infants with no major birth defects (controls) born between October 1997 through December 2004. Mothers reported dietary caffeine intake from coffee, tea, sodas, and chocolate in the year before pregnancy and reported intake of medications containing caffeine during pregnancy. Eleven percent reported consuming at least 300 mg of caffeine per day (2–3 cups/day) and 17 % reported consuming less than 10 mg of caffeine per day. The results did not suggest an association between maternal dietary caffeine intake and orofacial clefts, but caffeine-containing medications merit further study.

Another study comes from Norway, Department of Nutrition at University of Oslo. In Norway, coffee consumption is relatively high, reporting an average coffee intake for adult population (40–60 years old) of half a liter a day (Johansen et al. 2009). This study included 573 cases, 377 with CL/P and 196 with CPO and 763 randomly selected controls of infants delivered between 1996 and 2001. Mothers completed a 32-page questionnaire covering coffee intake, reported as number of cups per day, considering 100 mg of caffeine per cup as well as any medications and smoking and alcohol consumption during the first trimester of pregnancy. They found no evidence of an association between maternal coffee consumption during the first trimester and the risk of CPO, but there was a dose-response relationship with risk of delivering an infant with CL/P. The mechanism by which coffee intake might increase the risk of CL/P is not known, although the effects on homocysteine could be a potential pathway. Folic acid supplements reduce homocysteine plasma levels and reduce the risk of CL/P. Coffee intake, on the other hand, increases homocysteine levels (Grubben et al. 2000; Urgert et al. 2000), as well as smoking (Little et al. 2004), which is a well-established risk factor for CL/P (Johansen et al. 2009).

### **11.2.1.2 Neural Tube Defects (NTD)**

The National Birth Defects Prevention Study (NBDPS) is an ongoing multi-center population-based case control study of birth defects, which started on 1997 (Yoon et al. 2001). A subset of those participants, involving 306 mothers of NTD cases and 669 control infants and their parents were genotyped for CYP 1A2, the enzyme responsible for 95 % of caffeine metabolism. CYP 1A2 shows genetic polymorphism that reflects the bimodal distribution in the population (Sachse et al. 1999). The wild type, most common genotype is denoted by the presence of CYP 1A2\*1A

allele and the variant allele is when CYP 1A2\*1 F allele is present. The variant allele confers a slow caffeine oxidative phenotype and the wild type is associated with fast caffeine metabolism (Butler et al. 1989, Gu et al. 1992, Han et al. 2001). The purpose was to explore the association between NTDs and maternal and infant gene variants involved in caffeine metabolism. They found that maternal caffeine and its metabolites may be associated with increased risk for NTD-affected pregnancies in genetically susceptible subgroups. Caffeine-consuming mothers who were CYP 1A2 fast oxidizers, which are the most common genotype in the normal population, had non-significantly increased risk for NTD-affected pregnancy (Schmidt et al. 2010).

### 11.2.1.3 Cardiovascular Malformations (CVM)

Another subset from NBDPS population studied the consumption of caffeinated beverages (coffee, tea, colas, etc.) reported from 4196 CVM case infants overall and 3957 control infants (Browne et al. 2007). No significant positive association was found between maternal caffeine consumption and CVMs. On the contrary, an inverse trend between coffee intake and risk of atrial septal defect was observed.

On the contrary, animal studies on pregnant mice assessing both the short-term effects on cardiac development and embryo growth and long-term effects on cardiac function of *in utero* caffeine (coffee) exposure found different results (Wendler et al. 2009). In this study, animals were exposed to hypoxia (10 % O<sub>2</sub>) and treated with caffeine equivalent to the circulating levels in humans after 2 cups of coffee, from embryonic days 8.5–10.5. The hypothesis was that caffeine is an adenosine receptor antagonist and could disrupt adenosine protective action against hypoxia in utero, leading to acute effects on the embryo and long-term effects in adult mice. They found caffeine-induced effects on cardiac ventricle thickness in embryos and that effects on body composition (increased body fat) and cardiac function in adulthood were more greatly influenced by prenatal caffeine exposure.

Another recent study (Buscariollo et al. 2014) following the same methodology as the previous one, found that the observed altered cardiac function and morphology in adult mice exposed to caffeine (coffee) *in utero* was mediated by adenosine A1 receptors through DNA methylation. Differentially methylated regions within the genome were associated with cardiac hypertrophy.

### 11.2.1.4 Occurrence of Trisomy 21

A study involving a case-control of 997 liveborn infants with Trisomy 21 and 1007 liveborn controls without a birth defect between 1991 and 1993 in California was used to evaluate possible effects of maternal smoking and coffee (caffeine) consumption on the occurrence of a recognized pregnancy with Trisomy 21 (Torfs and Christianson 2000). An inverse association was found only for non-smoking mothers who drank  $\geq 4$  cups of coffee per day, suggesting that high coffee consumption is

more likely to reduce the viability of a Trisomy 21 conceptus than that of a normal conceptus.

A search of the MEDLINE/PUBMED from 1966 through October 2004 was made for all epidemiologic studies with maternal intake of caffeine as an exposure and major congenital malformations (Browne 2006). Their conclusion was that there is no evidence of teratogenic effect of caffeine in humans.

## ***11.2.2 Coffee, Pregnancy Loss and Birth Weight Reduction***

### **11.2.2.1 Spontaneous Abortion (SA)**

Studies from 1996 (Dlugosz et al. 1996) and 1997 (Fenster et al. 1997) investigated the use of caffeinated beverages (coffee, tea and soda) within 2967 and 5144 pregnant women respectively. Both studies concluded that as compared with abstention of caffeinated beverages, the adjusted odds ratios were increased for spontaneous abortion in association with three or more cups of coffee a day (>300 mg of caffeine). However, the first study could not identify the cause and attributed the effect to “some ingredient (or correlate) of coffee or tea that may account for the observed association” and the second study says that “we suspect that this association may be biased from relations among fetal viability, symptoms of pregnancy such as nausea, and consumption patterns during pregnancy.”

A review article recently published (Brent et al. 2011) covering period between 2000 and 2010 found that out of the 17 epidemiological studies dealing with the risk of SA from exposure to caffeine, only one actually measured the serum levels of caffeine and metabolites to determine the actual exposure. These authors noted that among these studies the results were inconsistent, some referring to levels of 300 mg or more of caffeine increasing the risk of SA and others reporting exposures of 500–900 mg of caffeine as not associated with risk of SA. The review concludes that when the wide range of human exposures have been utilized in animal reproductive studies, increased pregnancy loss in mammalian reproductive studies have not been detected.

### **11.2.2.2 Small for Gestational Age (SGA) and Pre-term Birth**

Caffeine is known to cross the placenta and reach the fetus and that the clearance of caffeine in the pregnant women is delayed (Chiapparino et al. 2006). Studies of coffee drinking and pre-term births have produced conflicting results, had limited information about caffeine sources, and did not control for any confounders. Parazzini and Chiffarino (Chiapparino et al. 2006) from University of Milan in Italy addressed this issue and found that 1966 women who gave birth at term ( $\leq 37$  weeks) used as controls and 502 who delivered early ( $\leq 37$  weeks) that there was an inverse association with coffee consumption in the 3rd trimester of pregnancy in the SGA cases compared with the normal gestational age. However, compared with the

non-coffee drinkers, a low consumption of coffee during pregnancy may not have significant effects on pre-term birth. A systematic review from Brazil (Pacheco et al. 2007) on caffeine consumption and prevalence of low birth weight and prematurity concluded that an association between moderate caffeine consumption and fetal growth was not demonstrated. The latest review and caffeine dose-response meta-analysis have found that the risk for low birth weight increased with increasing levels of caffeine intake (Chen et al. 2014). They found that the risk for low birth weight was significantly higher even in the low and moderate caffeine intake groups, 50–149 mg/day and 150–349 mg/day respectively, as compared with the reference group. Nonetheless, they cannot exclude the possibility for potential bias such as residual confounding for smoking and pregnancy symptoms. The current guideline by the WHO is to limit caffeine intake during pregnancy to a maximum of 300 mg/day (2–3 cups/day) and even more stringent are the Nordic Nutrition and American College of Obstetricians and Gynecologists recommendations to limit caffeine exposure to 200 mg/day (2010).

A review article on the evaluation of the reproductive and developmental risks of caffeine (Brent et al. 2011) has examined a number of epidemiological studies during the period of 2000–2010 on growth retardation in animals fed with caffeine (coffee). They concluded that the level of exposure necessary to produce fetal growth retardation to a pregnant women had to be significantly higher and far above the highest possible caffeine level of exposure which a pregnant woman would be exposed. They also concluded that there is a need for controlled trials to isolate cause and effect (Chen et al. 2014, Martin 2013; Pacheco et al. 2007).

### ***11.2.3 Maternal Coffee Intake and Potential Complications***

#### **11.2.3.1 Gestational Diabetes Mellitus (GDM)**

The Epidemiology Branch at the Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institute of Health, Bethesda, MD examined a population of non-diabetic women with singleton pregnancies in the Danish National Birth Cohort (n=71,239) and estimated the relative risks for the association between first trimester coffee and tea intake or estimated total caffeine intake and GDM. Their results suggest that moderate first trimester coffee and tea consumption were not associated with GDM increased risk; on the contrary it could have a protective effect (Hinkle et al. 2014).

#### **11.2.3.2 Anemia and Iron Deficiency**

There are reports of findings from the 1980s in rats (Munoz et al. 1986) and among pregnant women and their infants (Munoz et al. 1988), which indicated that maternal coffee intake may contribute to maternal and infant anemia due to iron

deficiency. Animal studies also investigated the effect of coffee consumption and the absorption of zinc and iron (Morck et al. 1983; Pecoud et al. 1975). The results suggested a significant reduction in the zinc and iron absorption due to coffee intake. A review article on the consequences for the newborn of chronic coffee consumption during gestation and lactation concluded (Nehlig and Debry 1994) that maternal caffeine consumption in moderate amounts ( $\leq 300$  mg of caffeine equivalent to 2–3 cups a day) has no measurable consequences in the fetus and newborn infant. No recent studies were found to confirm those previous results. It is possible that the increased addition of important minerals to cereals and the required use of vitamins and minerals supplementation during pregnancy might have adjusted those increased needs during gestation and in the infants.

### 11.2.3.3 Febrile Seizures

Febrile seizures are quite common during childhood, caused by genetic or environmental factors in early life. The association of maternal coffee intake and exposure to cigarettes and alcohol was evaluated by the Aarhus Birth Cohort consisted of 25,196 children of mothers scheduled to deliver between 1989 and 1996 (Vestergaard et al. 2005). No association was found between maternal coffee intake during pregnancy and risk of febrile seizures.

### 11.2.3.4 Primary Sclerosing Cholangitis (PSC)

A recent study from Norway on maternal coffee consumption, smoking and hormones and the risk of PSC was published (Andersen et al. 2014). They observed 240 patients with PSC from Oslo University Hospital and they concluded that coffee consumption and smoking can actually protect against development of PSC.

### 11.2.3.5 Coffee Effects on Adult Son's Semen Quality

Association between prenatal coffee, current caffeine exposure and semen quality and levels of reproductive hormones was evaluated in 347 sons out of 5109 selected for a follow-up study from The Danish Pregnancy Cohort. Semen and blood samples were analyzed (Ramlau-Hansen et al. 2008). Caffeine intake was shown to be associated with increased levels of testosterone, but no clear association was found with semen quality. Another study with a subset of The Child Health and Development Studies involving the participation of 338 adult sons from a follow-up study where 196 participants donated semen for analysis (Cirillo et al. 2011). Semen samples were analyzed for sperm concentration, motility and morphology. It was found a proportionate 25 % reduction on sperm count, 13 % decrease in motility and 25 % decline in the normal morphology. Those studies provide suggestive evidence that maternal coffee use during pregnancy may impair the

reproductive development of the male fetus. However, those results were from a very high prenatal exposure, corresponding to 5 cups of coffee use per day, much higher than the recommended dose of no more than 2 cups per day during pregnancy.

### 11.2.3.6 Strabismus

A review of medical records for children in the Danish National Birth Cohort identified 1321 cases of strabismus from a total of 96,842 children born between 1996 and 2003 (Torp-Pedersen et al. 2010). Maternal smoking was associated with a significantly elevated risk of strabismus, light maternal alcohol consumption was associated with decreased risk and no association was found with maternal coffee or tea drinking.

## 11.2.4 *Coffee and Risk of Cancers*

### 11.2.4.1 Childhood Acute Leukemia

Epidemiological studies on the association between coffee consumption during pregnancy and childhood acute lymphoblastic leukemia (ALL), the most common subtype among acute leukemia in US, have been inconsistent (Cheng et al. 2014). Two French population-based case control studies from 2005 (Menegaux et al. 2005) and 2007 (Menegaux et al. 2007) concluded that over 280 incident cases and 288 controls that maternal coffee consumption during pregnancy was associated with childhood acute leukemia, ORs increasing in ALL with coffee consumption (OR=1.1 [0.7–1.8], OR=2.4 [1.3–4.7] and OR=3.1 [1.0–9.5]), respectively, for <or = 3, 4–8 and >8 cups/day. The latter, otherwise, concluded that maternal coffee consumption was not significantly related to AL. Only the highest intake of coffee ( $\geq 3$  cups/day) had a significant correlation with mothers that were also non-smokers, over a population of 472 of AL cases and 567 case controls. A recent meta-analysis study published on American Journal of Obstetrics and Gynecology (Chen et al. 2014) on this particular issue has concluded that it is suggestive of an increase in the risk of ALL with maternal coffee consumption. They found a linear dose-response relationship between coffee consumption and childhood AL.

Caffeine may act as a topoisomerase II inhibitor, a DNA repair inhibitor or a carcinogen metabolism inhibitor (Ferguson and Philpott 2008; Ross et al. 1996). These actions could induce chromosomal translocations and aberrations, such as on chromosome 11q23, which was taken as a cause for the pathogenesis of infant leukemia (Ross et al. 1996). However, it is our understanding that the inconsistency found in the studies might be attributable to the complex chemistry of coffee and to other compounds present in much higher concentration in coffee, such as the chlorogenic acids (CGA's) (Santos 2010).



#### 11.2.4.2 Coffee Constituent Chlorogenic Acid and Cancer Prevention

Coffee is the major dietary source of chlorogenic acids (CGA's), a 200 mL cup is reported to contain a range from 70 to 350 mg, much higher than the amount of caffeine (Burgos-Moron et al. 2012). CGA's have been known for their antioxidant properties (Kono et al. 1997; Sato et al. 2011). Burgos-Moron's group of researchers reported for the first time that CGA induces high levels of topoisomerase I and topoisomerase II-DNA complexes in cells. Topo I and topo II are nuclear enzymes that introduce single- or double-strand breaks in the DNA to solve topological problems associated with DNA replication, transcription, recombination and chromatin remodeling. Their study showed that lung cancer cells were more sensitive than normal lung fibroblasts to the cytotoxic activity of CGA, suggesting that CGA may induce selective killing of cancer cells and consequently a possible cancer preventative activity.

#### 11.2.4.3 Coffee and Risk of Testicular Cancer

It has been suggested that increased risk for testicular cancer in the world may be due to exposures during fetal development (Bray et al. 2006; Maffezzini 2007; Huyghe et al. 2003). The Child Health and Development Studies, a 40-year follow-up of more than 20,000 pregnancies between 1959 and 1967 found only 20 cases of testicular cancer diagnosed through 2003 among sons with a maternal interview during pregnancy. Compared with controls, mothers of testicular cancer cases were more likely to drink alcohol and less likely to drink coffee (Mongraw-Chaffin et al. 2009).

### 11.3 Coffee Effects in Infancy and Early Childhood

Caffeine is a widely used psychoactive substance by both adults and children. It is classified as a stimulant drug that is typically used for its ability to arouse the central nervous system. Children and adolescents are the fastest growing population of caffeine users with an increase of 70 % in the past 30 years (Harnack et al. 1999). This section will review the effects of the use of caffeine-containing beverages (coffee, tea, chocolate, soft drinks) on the behavior and development of children.

It is important to recall that although coffee is the main source of caffeine in the adult diet, it seems that soft drinks is the preferred route of caffeine administration by children and adolescents (Frary et al. 2005). Much of the data from the studies that this section will cover will be a reflection of their drinking habits and not directly related to coffee consumption.

A review of effects of caffeine on development and behavior in infancy and childhood, published in 2002 by researchers from the National Institute of Mental Health, NIH, Bethesda (Castellanos and Rapoport 2002), examined studies found in

the literature in the previous decade. They found that the number of papers indexed were small; in consequence they have attributed this scarce literature to the continued practice to recommend women to moderate coffee consumption. They reported a few positive associations such as gestational coffee drinking linked to iron deficiency in children (Engle et al. 1999) and heavy caffeine intake ( $\geq 400$  mg/day) associated with increased risk of sudden infant death syndrome (SIDS) (Ford et al. 1998). Overall the results were beneficial, such as that children reported fewer adverse effects while exhibiting greater objective changes in activity and task performance (Rapoport et al. 1981). Additionally a meta-analysis of 9 studies with 96 children with Attention Deficit/Hyperactivity Disorder (ADHD) showed a beneficial effect on parental ratings of aggressive or disruptive behavior (Stein et al. 1996). Finally the report concluded that there was little evidence that would warrant grave concern about the use of moderate doses of caffeine in most situations and that the effects of caffeine in children seem- to be modest and generally innocuous.

Animal studies looking at chronic caffeine treatment during the pre-pubertal period in adult spontaneously hypertensive rats (SHR), an animal model for the study of ADHD, demonstrated for the first time that caffeine or methylphenidate (Ritalin™) improved cognitive deficits in adulthood (Pires et al. 2010). Methylphenidate is the most accepted pharmacological treatment for ADHD. However, its use during adolescence may cause long-lasting neurobiological developmental consequences in rodents. In this case, the search of an alternative/complimentary treatment such as caffeine could be of help.

The effect of caffeine and technology on sleep duration and body mass index was the focus of a study with 625 children aged between 6 and 20 years old, from the National Sleep Foundation's Sleep in America Poll (Calamaro et al. 2012). The study found that on a typical day around 30 % of the children consumed a cup or can of caffeinated beverage, almost half of the sample had a television in their bedroom and 10 % or fewer had a computer and a phone. Children averaged 9.5 h of sleep each night, even though children aged between 6 and 10 years need 10–11 h of sleep per night. A complex relationship between caffeine intake and the use of technology such as television and computers in the bedroom was found. Shortened sleep (15 min less) was associated with drinking a cup of caffeinated beverage, but greater loss of sleep (45 min less, on average) was found when 2 other items were present: television and computer. However, no individual technology item influenced the hours of sleep the child obtained.

Another review on caffeine use in children published in 2009 (Temple 2009) discussed probable mechanisms for the caffeine effects seen in adults as well as in children, mainly through its binding to adenosine receptors in the brain. The main concern is the fact that children and adolescents are still developing some parts of the brain. Some of these areas such as orbitofrontal and temporal lobes (Giedd 1999; Sowell et al. 1999) contain adenosine receptors that can be potentially affected by caffeine (Svenningsson et al. 1997). However, the data available regarding caffeine use in children is very scarce and do not allow drawing any solid conclusions. More research needs to be conducted in this area.

## **11.4 Coffee Effects in Adolescence**

### ***11.4.1 Effects of Acute Doses of Caffeine in Adolescents***

Acute administration of doses of 50, 100 and 200 mg of caffeine (equivalent to 1–2 cups of coffee, 100 mg of caffeine per cup on average) to a group of adolescents followed by monitoring cardiovascular responses (blood pressure) and food intake has been performed (Temple et al. 2010). The main effects of an acute caffeine dose was on heart rate (HR) and diastolic blood pressure (DBP), with HR decreasing but DBP increasing with increasing caffeine dose. High caffeine consumers (>50 mg/day) reported to use caffeine to stay awake in the form of coffee, tea, sodas and energy drinks. Boys were more likely than girls to report use of caffeine for a “rush” or simply for more energy or exercise performance. They concluded that the acute effects of caffeine in adolescents are moderated by gender and frequency of caffeine use.

### ***11.4.2 Effects of Acute and Chronic Dosing of Caffeine in Animals***

Rats undergo developmental changes in the brain during adolescence with many parallels to human brain development during the comparable stage (Crews et al. 2007, Spear 2000). Therefore, adolescent rats are a valuable model in exploring interactions of drugs with the development of the brain. A study used rats on the 28th postnatal day-of-age (P28) to test as adolescents and in the age-range between P65 to P95 to test as young adults (Rhoads et al. 2011). The purpose of the study was to examine the effects of acute and chronic dosing of caffeine in adolescent rats and compare with adult rats. Their results showed that adolescent rats present similar responses to the initial acute dose of caffeine but showed greater signs of tolerance and dependence than adults after regular coffee consumption. They concluded that adaptive changes such as tolerance and withdrawal symptoms may be occurring faster or to a greater extent in the still-developing adolescent brain.

### ***11.4.3 Coffee and Weight Gain***

A subset of 5502 girls from the Growing up Today Study from all over U.S. aged 14–21 year., returned surveys in 2001 reporting the past-year recreational Internet time, sleep, coffee (with caffeine) and alcohol consumption. Their height and weight were also reported in 2000. The investigators examined whether excessive recreational Internet time, insufficient sleep, regular coffee and/or alcoholic beverages consumption promote weight gain (Berkey et al. 2008). They found that females aged 18+ years presented a high correlation between more Internet time, more

alcohol and less sleep with same year BMI increase. The study also found no evidence that drinking coffee promotes weight gain.

Some studies were looking at coffee and other caffeine containing beverages consumption concerned with the establishment of future habits in adult life that could lead to disorders such as diabetes and obesity (Koivusilta et al. 2001; O'Dea and Wilson 2006). Koivusilta et al. (2001) concluded that poor dietary choices (high consumption of soft drinks, sweets, snack foods, take away and large food portions) were associated with a high BMI in children and adolescents and in adult life. The findings were most notable in those who either skipped breakfast and/or prepared a breakfast of poor nutritional quality (Ortega et al. 1998). O'Dea in her study also looked at educational background and socioeconomic status (SES) in a large (n=4441) national study of school children aged 6–18 years. (O'Dea and Wilson 2006). In this study, non-nutritious fluids were considered as soft drink, water, coffee and tea; and that students with low SES were more likely to skip breakfast or to consume a non-nutritious breakfast instead. Boys and girls of low SES as compared with middle/high SES had significantly greater BMI and consequently greater risk of overweight and obesity.

#### ***11.4.4 Coffee Consumption and Vitamin D***

The effects of coffee (caffeine) consumption and levels of vitamin D are controversial. It has been demonstrated that caffeine negatively influences calcium balance by reducing renal reabsorption of calcium (Massey and Whiting 1993). Another study found that methylxanthine, theophylline and caffeine inhibit the conversion of 25-hydroxyvitamin D3 to 1,25-dihydroxyvitamin D3 in the renal tubules of vitamin D deficient chicks, leading to an increase in the vitamin D circulating levels (Taft et al. 1984). Moderate coffee consumption has no effect on bone health (Massey and Whiting 1993). A recent study with 330 randomly selected Saudi adolescents aged 11–14 years. from the existing Biomarkers Screening in Riyadh Program found that serum vitamin D levels increases as coffee and tea consumption increases; and that increase is independent of physical activity, sun exposure, gender, age and BMI (Al-Othman et al. 2012).

#### ***11.4.5 Effects of Caffeine on Sleep Disorders in Animals***

Caffeine is a CNS stimulant known to affect sleep-wake regulation (Fredholm et al. 1999; Schwierin et al. 1996). Adolescence is a critical period for brain maturation in which a huge reorganization of cortical connectivity takes place. A study with the purpose of establishing a rat model to assess the relationship between cortical maturation and sleep utilized caffeine as a short-term stimulant (Olini et al. 2013). The amount of caffeine administered to the rats was equivalent to 3–4 cups of coffee a

day (100 mg caffeine/cup of coffee on average). The study showed that caffeine interferes with cortical maturation during adolescence in rats, a critical period of brain development. Also these results might be of clinical importance since the critical period of synapse elimination during adolescence is associated with increased incidence of psychiatric and mood disorders such as schizophrenia, anxiety, substance of abuse and personality disorders.

## 11.5 Conclusion

The majority of the literature reviewed in this section was related to the effects of caffeine in the early stages of human life, during pregnancy, neonates and early childhood; and the major concern being the possible damage to the various phases of child development.

The studies that involved those periods of human development referred to number of cups of coffee as the major source of caffeine in the adult diet. Some controversial results are still present, due to the lack of data in terms of type of caffeinated beverage (coffee/tea/sodas), type of coffee (caffeinated/decaffeinated) and correlation with *in vivo* levels of caffeine in the body. Nevertheless, the majority of the studies presented here concluded that coffee was not related with any of the adverse effects or development of diseases focused on the respective research papers. On the contrary, there were some studies that concluded that coffee in moderation is good for health.

As we move into late childhood and adolescence, the major source of caffeine is not coffee, but sodas and energy drinks. The number of papers are considerably smaller and the results cannot be attributed to coffee consumption, reason why they were not addressed in this chapter (Bernstein et al. 1994, 2002; Oberstar et al. 2002; Orbeta et al. 2006; Reissig et al. 2009). Many more studies are still necessary in order to better clarify those questions that continue unanswered. In the meantime, the best advice remains to use coffee/caffeine in moderation and enjoy your early morning beverage without guilt (Santos and Lima 2009).

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