Biological Effects of Caffeine on the Brain

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Why I Chose to Write on My Topic

The addiction to the deceiving drug known as caffeine has been an issue for many years of my life. The addiction was not apparent to me until I experienced serious withdrawal symptoms. In the past, I would starve myself to the extent that I felt the need for a low-calorie alternative to get me through the day. I was pleased with the effects of caffeine for a short while, until I unfortunately become dependent. I knew that caffeine was not beneficial to most, if not all of the human body. I unfortunately ended up with kidney stones, caffeine being the primary cause. I had no idea that caffeine was damaging to the organs of the body until this unfortunate event. As a dehydrator, caffeine caused my kidneys to have difficulties breaking down the calcium-oxalates in my kidneys, therefore they formed stones and were passed undiluted.

Those who feel a need for caffeine regularly tend to defend their habit by striving to make their addiction appear beneficial. This is also known as denial. We all know that caffeine is not an advantageous chemical to ingest as it is hard on the liver, kidneys, and heart, but not many are aware of the biological effects it has on the brain. I have heard that caffeine can be beneficial in small doses to the brain.

As an athlete, I am always looking for better ways to improve my performance. What I choose to put in my body not only will affect my energy level physically, but mentally as well. Caffeine may give someone a short burst of energy, but results in a hard crash later. Even though I am able to study longer with this stimulant in my system, I try not to ingest large quantities as I am aware of the severity of the withdrawal symptoms when addicted. Many people live for the here and now, rather than the future, which is largely why they allow these addictions to become
a part of their lifestyle. I hope that by furthering my knowledge of the effects of caffeine on the brain, I will be better able to determine whether or not it is beneficial and what for. If it is beneficial, I would like to know whether or not it is worth it to ingest caffeine as it may do more damage than good.

I am also aware, as a woman, that it is dangerous to ingest caffeine when pregnant. It is understood that caffeine is a vasodilator, but I am curious as to whether or not it is more beneficial than it is harmful in terms of harming the fetus versus benefiting the brain of the mother and or fetus.

**What the Research Says About My Topic**

Caffeine is the number one ingested psychoactive drug by the human race. When this substance is consumed, it has many biological effects on the brain. The hippocampus of the brain is influenced in a positive way for those who suffer from Type I diabetes (Duarte, Carvalho, Cunha, & Gruetter, 2009). The caffeine has been proven to prevent hippocampal degeneration and memory dysfunction, as well as positively influencing the peripheral glucose metabolism. This study showed that the hippocampal glucose content and function were not affected in diabetic rats, irrespective of caffeine consumption (Duarte et al., 2009). Compared to the control group, the diabetic rats that consumed caffeine “displayed increased hippocampal levels of myo-inositol (15 ± 5%, p < 0.05) and taurine (23 ± 4%, p < 0.01), supporting the ability of caffeine to control osmoregulation” (Duarte et al., 2009, p.1). The caffeine consumption prevented synaptic degeneration and astrogliosis (Duarte et al., 2009). “In conclusion, neurochemical alterations in the hippocampus of diabetic rats are not related to defects of glucose transport but likely reflect osmoregulatory adaptations caused by hyperglycemia” (Duarte et al., 2009, p.1). Caffeine had an
effect on the neurochemical adaptation to high glucose levels, which can relate to its neuroprotective effects, particularly preventing synaptic degeneration and astrogliosis (Duarte et al., 2009). Astrogliosis is an abnormal increase in the number of atrocities due to the destruction of nearby neurons, typically because of hypoglycemia or oxygen deprivation.

Caffeine has also been found to prevent age-associated recognition memory decline (Costa, Botton, Mioranzza, Souza, & Porciúncula, 2008). An evaluation was done on mature mice ranging from young adult to old age on recognition memory using the object recognition task (Costa et al., 2008). The adult mice were 6 months old and the aged were 18 months (Costa et al., 2008). Both control groups were tested for object recognition task without any caffeine and the results concluded that the 18 months old mice “exhibited lower performance in the recognition memory” (Costa et al., 2008, p.1). The aged group of mice that were given caffeine showed similar performance to the control group of young adult mice in the objection recognition task (Costa et al., 2008). These results agree with other studies and assure that caffeine consumed in adulthood can prevent recognition memory decline as one ages (Costa et al., 2008).

Alzheimer’s disease is a very difficult disease to live with. Recent studies suggest that caffeine may help protect against this unfortunate disease. Studies have shown that a moderate amount of caffeine can protect and or restore cognitive function and slows down the production of amyloid-β in those suffering from Alzheimer’s disease (Chuanhai, Cirrito, Xiaoyang, Wang, Verges, Dickson, Mamcarz, Chi, Mori, Arendash, Holtzman, & Potter, 2009). Amyloid-β is a peptide of 39 to 43 amino acids that appear to be the main component of amyloid plaques in the brains of
Alzheimer's disease patients. The results indicated that caffeine reduces the amyloid-β levels in both the plasma and the brain, indicating a positive effect of caffeine (Chuanhai et al., 2009).

Parkinson’s disease can also be positively influenced by caffeine. Recent studies have shown that caffeine can help protect the brain from developing Parkinson’s disease (Nakaso, Ito, & Nakashima, 2008). “Caffeine activates the P13K/Akt pathway and prevents apoptotic cell death in a Parkinson’s disease model of SH-SY5Y cells” (Nakaso et al., 2008, p.1). Caffeine was found to prevent the apoptotic cell death that is triggered by “serum/retinoic acid (RA) deprivation, MPP+, rotenone, and 6-OHDA in SH-SY5Y cells in a dose dependent manner (Nakaso et al., 2008, p.1). Caffeine also lowered caspase-3 activity that is caused by serum/RA deprivation and 6-OHDA administration, and decreased the number of apoptotic condensed and/or fragmented nuclei as well (Nakaso et al., 2008). Akt was phosphorylated 60min after caffeine administration in a dose dependent manner; PI3K inhibitors, wortmannin and LY294002 canceled this cytoprotective effect of caffeine. On the other hand, MAPKs such as Erk1/2, p38, or JNK were not activated by caffeine. The results indicated that the caffeine had a “cytoprotective effect due to the activation of the PI3K/Akt pathways in SH-SY5Y cells” (Nakaso et al., 2008, p.1).

There have been mixed reviews on whether or not caffeine protects the brain from high-fat diets. A recent study was done on rats to discover the biological effects of caffeine on the brain of someone with a high-fat diet. The high amounts of insulin secreted as well as the fat of the mice on these diets were suppressed when given caffeine (Unno, Yamamoto, Maeda, Takabayashi, Yoshida, Kikunaga, Takamori, Asahina, Iguchi, Sayama, & Hoshino, 2009). “Furthermore, brain atrophy was suppressed and the working memory, tested using Y-maze,
improved in mice fed a high-fat diet containing green tea catechin and caffeine” (Unno et al., 2009). The working memories of the mice treated with this diet were improved. The results concluded that the brain atrophy was abated and the memory was enhanced when the ingestion of caffeine took place (Unno et al., 2009). Caffeine consumption is not only beneficial to the memory part of the brain, but to the stabilization of the blood-brain barrier as well. The blood-brain barrier is vital for brain homeostasis, and can cause several neurological disorders if disrupted (Xuesong, Ghribi, & Geiger, 2007). Recent studies were done on New Zealand rabbits to test the hypothesis that caffeine protects against disruption of the blood-brain barrier (Xuesong et al., 2007). This study showed that when the caffeine is ingested regularly, it protects against a number of neurological disorders, unfortunately we have very little understanding of these mechanisms (Xuesong et al., 2007). The results suggest that caffeine in a stabilizer of the blood-brain barrier by restricting vascular inflammation (Xuesong et al., 2007). In other words, swelling that can affect the blood-brain barrier is stabilized by the infusion of caffeine.

Caffeine has been found to reduce the initial dip in the visual blood oxygenation level-development (BOLD) response with the use of an MRI (Behzadi & Liu, 2006). “In this study, the BOLD response to a 4-s long visual stimulus was measured with a 3-T MRI system in 5 healthy volunteers both before and immediately after a 200-mg oral caffeine dose. The caffeine dose significantly (P < 0.001) reduced or eliminated the initial dip in all subjects” (Behzadi & Liu, 2006, p.1). This indicates that caffeine can positively affect the initial dip in the MRI studies (Behzadi & Liu, 2006).

The biological effects of caffeine on the brain are favorable for those suffering from severe traumatic brain injuries. Studies have shown that caffeine is a "neuroprotective substance
by long-term upregulation of adenosine A1 receptors” (Sachse, Jackson, Wisniewski, Gillespie, Puccio, Clark, Dixon, & Kochanek, 2008, p.2). Serial cerebrospinal fluid concentrations of caffeine and its metabolites such as theobromine, paraxanthine, and theophylline were assessed during this study (Sachse et al., 2008). This assessment was done with “high-pressure liquid chromatography/ultraviolet in 97 ventricular CSF samples from an established bank, from 30 adults with severe TBI” (Sachse et al., 2008, p.1). They chose a threshold caffeine level of ≥1 μmol/L (194 ng/mL) as clinically significant (Sachse et al., 2008). “Demographics, Glasgow Coma Scale (GCS) score, admission blood alcohol level, and 6-month dichotomized Glasgow Outcome Scale (GOS) score were assessed” (Sachse et al., 2008, p.1). From injury to initial CSF sampling was 10.77±3.13 h (Sachse et al., 2008). Caffeine was detected in 24 of 30 patients, and the threshold was achieved in 9 patients for the initial sampling (Sachse et al., 2008). Gender, age, admission CGS score, admission blood alcohol level, and admission systolic arterial blood pressure did not differ between patients with CSF caffeine concentration ≥ versus < the threshold. The metabolites as well as the caffeine itself are often found in CSF in patients that suffer traumatic brain injury and are associated with positive outcomes (Sachse et al., 2008). In conclusion, chronic caffeine ingestion has been found to attenuate brain injury, “by A<sub>1</sub> receptor-mediated suppression of the glutamate releaser and inhibition of excess inflammatory cytokine production” (Li, Dai, An, Li, Chen, Xiong, Liu, Wang, Zhao, Zhu, Liu, Zhu, Chen, & Zhou, 2008, p.2). Caffeine therefore, can positively influence the brain of those with traumatic brain injuries by reducing inflammation.

On a more negative note, caffeine can prohibit one from sleeping when it is necessary. A study was done to test the hypothesis of adenosine’s involvement in the induction of sleep after
prolonged wakefulness (Elmenhorst, Meyer, Winz, Matusch, Ermert, Coenen, Basheer, Haas, Zilles, & Bauer, 2007). The scientists used “the highly selective A1 adenosine receptor (A<sub>1</sub>AR) radioligand [<sup>18</sup>F]CPFPX ([<sup>18</sup>F]-cyclopentyl-3-(3-fluoropropyl)-1-propylxanthine) and quantitative positron emission tomography to assess cerebral A1ARs before and after sleep deprivation in 12 healthy volunteers and a control group (n = 10) with regular sleep (Elmenhorst, et al., 2007, p.1). As caffeine has been discovered as a nonselective blocking substance of adenosine receptors, “the sleep deprived subjects were found with an “increase of the apparent equilibrium total distribution volume in a region-specific pattern in all examined brain regions with a maximum increase in the orbitofrontal cortex (15.3%; p = 0.014)” (Elmenhorst et al., 2007, p.1). The control group showed no changes with regular sleep (Elmenhorst et al., 2007). This study is the first molecular imaging study that provides in adequate research for an “A<sub>1</sub>AR upregulation in cortical and subcortical brain regions after prolonged wakefulness, indicating that A<sub>1</sub>AR expression is contributing to the homeostatic sleep regulation” (Elmenhorst et al., 2007, p.1). Therefore, caffeine is not recommended for those with mild to severe sleep irregularities.

Rats with motor function disabilities were treated with caffeine in order to observe the effects it had on them and whether they were positive or negative. “The effects of chronic oral treatment with low doses of caffeine (1–3 mg/kg) and trihexyphenidyl (0.1–0.2 mg/kg) were tested on hemiparkinsonian rats, which received the following treatments in a counterbalanced order: vehicle, caffeine, trihexyphenidyl, and caffeine plus trihexyphenidyl” (Bata-García, Villanueva-Toledo, Gutiérrez-Ospina, Álvarez-Cervera, Heredia-López, & Góngora-Alfaro, 2007, p.1). Three models consisting of the stepping test, the cylinder test, and the staircase tests
were all used in this experiment. The stepping test showed a complete recovery of motor function in both doses (Bata-García et al., 2007). The cylinder test revealed that “only the wall contacts performed simultaneously with both forepaws were significantly increased by caffeine (3 mg/kg)” (Bata-García, et al., 2007, p.1). The staircase test showed no improvement in the food pellet retrieval with the contralateral forepaw when the rats were given caffeine (Bata-García, et al., 2007). The overall results concluded that consistent amounts of caffeine given to rats in doses close to human consumptions produces an improvement that is consistent in the use of the “contralateral forelimb in unilaterally 6-hydroxydopamine enervated rats, without the development of tolerance” (Bata-García et al., 2007, p.1). These results suggest that caffeine can be therapeutic and can help those with Parkinson’s disease reverse the motor symptoms they suffer from (Bata-García, et al., 2007). Caffeine has an amazing effect on hemiparkinsonian rats and can be a legitimate reason for humans suffering from these symptoms to take small amounts of caffeine into consideration.

Caffeine has been hypothesized to help regulate the methylmercury (MeHg) toxicity in the brain by being the antagonist to the adenosine receptor system (Björklund, Kahlström, Salmi, Ögren, Vahter, Chen, Fredholm, & Daré, 2007). “Behavioral outcomes of low dose prenatal MeHg exposure were studied in mice where the A$_1$ and A$_{2A}$ adenosine receptors were either partially blocked by caffeine or eliminated by genetic modification (A$_1$R and A$_{2A}$R knock-out mice) (Björklund et al., 2007, p.1). From gestational day 7 to day 7 of lactation dams were given doses that were equivalent to the average human diet i.e. 1µM MeHg and/or 0.3g/l caffeine in the drinking water (Björklund et al., 2007).. This exposure to MeHg resulted in a doubling of brain Hg levels in
wild type females and males at postnatal day 21 (PND21)” (Björklund et al., 2007, p.1). The caffeine ingested by the mothers resulted in long-lasting changes in the offspring, shown through the increased motor activity and results to psycho stimulants (Björklund et al., 2007). Similar differences were discovered in A<sub>1</sub>R knock-out mice, meaning that adenosine A<sub>1</sub>R is related to the alterations triggered by caffeine exposure during development (Björklund et al., 2007). Prenatal caffeine dosages attenuated the behavioral consequences of MeHg in male mice (Björklund et al., 2007). The inactivation of the adenosine A<sub>1</sub>R receptors through the use of caffeine also related to the positive effects caffeine has on hypoxia and Parkinson’s disease (Björklund et al., 2007). In conclusion, the negative outcomes of MeHg toxicity during gestation and lactation can be eliminated or reduced by the inactivation of the adenosine A<sub>1</sub>R and A<sub>2A</sub> receptor, by the ingestion of their antagonist caffeine (Björklund et al., 2007). While caffeine intake is generally discourages during pregnancy, in the case of mercury poisoning the positive effects on the brain may outweigh the negative for the fetus.

Many Scientists have wondered about the effects of caffeine on the quantitative parameters of the EEG and ultraslow electrical processes in the brain. “A study of the power and coherence of the ultraslow phasic processes (USPPs) of the brain in the frequency range 0.05–0.5 Hz and the EEG (1.5–50 Hz) at rest with the eyes opened or closed before and after the administration of caffeine and was performed” (Boitsova & Dan’ko, 2007, p.1).

Electroencephalography (EEG) is the recording of electrical activity along the scalp produced by the firing of neurons within the brain. EEG refers to the recording of the brain's spontaneous electrical activity over a short period of time, usually 20–40 minutes, as recorded from multiple
electrodes placed on the scalp. During this study, caffeine caused changes in the EEG pattern (Boitsova & Dan’ko, 2007). The USPP data shows that the differences in the drug effects are impacted not only by the different topography changes in the USPP pattern, but also by an opposite direction of these changes (Boitsova & Dan’ko, 2007). “This fact makes it possible to suppose that, during pharmacological tests, the differential sensitivity of USPPs as an indicator of CNS sensitivity may be higher than that of the EEG, in view of the closer relationship between the behavioral and electrographic changes” (Boitsova & Dan’ko, 2007, p.1). In conclusion, the electrical activity of the brain is increased by caffeine, resulting in enhanced brain performance.

What I Learned Personally, Interpersonally, and Professionally

After I completed the research on this topic, I realized that there are a few positive effects caffeine can have on my brain. Small amounts of caffeine that are found in things such as green tea can help improve my memory. This could be beneficial scholastically for me as long as the dosages are small. I would not want to become addicted, nor do I want to damage my other organs, so I would be sure to consume small quantities from natural sources such as tea. I realize that the brain may not be negatively affected, but the rest of my body can be, therefore it is unwise to ingest caffeine as it can do more harm than good.

I learned interpersonally that people can actually abuse the drug, but if they take small quantities, it can help them reduce the symptoms of many diseases. My grandmother for example, suffers from Parkinson’s disease and migraines. As she gets older, it might be beneficial for her to drink a cup of tea a day to suppress some of the symptoms as well as improve her memory. It is unfortunate that this disease allows one to become off balance and unstable. My grandfather also tends to forget things more often, and some are crucial. I’d like to
be assured that he will remember to take his medication when there is no one there to remind him.

I learned professionally that caffeine does help sustain my memory when tutoring. Small amounts assist me in keeping me sharp in math when teaching my students. Those who drink a cup of coffee a day also tend to retain lots of information. At times I forget how to do basic algebra, as I haven’t done it in several years. I would not depend on caffeine by any means, but to have a cup of tea once a day may be good for my memory as well as insulin secretion.

**How I Plan to Apply What I Learned Personally, Interpersonally, and Professionally**

I plan to apply what I learned personally by recognizing what caffeine is doing to my brain and why. If I do decide to ingest any amount of this stimulant, I will have small quantities for the beneficial effects it has biologically on the brain only. I will not exceed one cup of tea a day and I will be sure not to allow it to become an addiction. I will have a cup at different times each day to keep my brain and body from becoming dependent on it to function.

I plan to apply what I learned interpersonally by helping others understand the biological effects caffeine can have on their brain. I will accept limited amounts of caffeine into my friend’s and family members’ lifestyles as long as they recognize that the brain may not be harmed, but other organs of the body can and will be. I also will be a little more accepting of people that drink one cup of tea or coffee a day; however I will always suggest tea. Tea has less caffeine than coffee and is closer to the more appropriate amount for the average person.

Professionally, I plan to apply what I’ve learned by keeping in mind that those ingesting limited amounts of caffeine may retain what I teach them better, especially the older students. I will recommend more sleep before caffeine, but small amounts of caffeine can improve the
retention of information, therefore small portions will be tolerated. Those who work hard do not need the drug caffeine to achieve their goals scholastically, as it only helps in limited amounts; it is not a miracle worker. The more caffeine one ingests, the more damage that is being done to overall. Drink responsibly. As with many things, the key is to use in moderation, and not excess.
References


